# consultant

May 1961

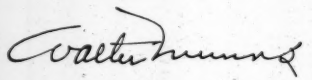


SK&F

This is the second issue of CONSULTANT, a monthly medical magazine SK&F is publishing for practicing physicians.

As we said in the first issue, there are several things about CONSULTANT we think you will like—articles that are short and to the point, Questions and Answers that challenge and summarize.

Beginning with the third issue there will be another feature—a Correspondence Section, in which the Consultants will try to answer your questions about their topics. So if you have a question about something they have said in their articles, send it as soon as you can. The authors will answer all questions by mail; we will publish some of them in subsequent issues. All questions should be addressed to CONSULTANT, Smith Kline & French Laboratories, 1500 Spring Garden Street, Philadelphia 1, Pennsylvania.



Walter A. Munns, President

consultant
May 1961



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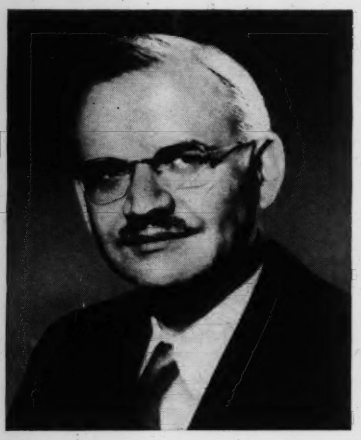
# GYNECOLOGY



**William F. Mengert, M.D.**
**University of Illinois**

*William F. Mengert is Chairman of the Department of Obstetrics and Gynecology at the University of Illinois College of Medicine. He received his medical degree at Johns Hopkins Medical School and was intern and resident at the University of Iowa Hospitals, where he later joined the senior faculty of the medical school. From there he went to the Southwestern Medical School in Dallas. He has served as president of the American College, the American Association, and the Central Association of Obstetricians and Gynecologists. He was also chairman of the Section on Obstetrics and Gynecology of the American Medical Association. He is author of a textbook and over 100 scientific papers.*

## OFFICE GYNECOLOGY: SOME POINTS TO REMEMBER

"Office Gynecology" is a popular subject at most general medical meetings because so many physicians realize its elusive aspects. The average physician tends to suspect that his female patients are dissatisfied with the advice and treatment he gives, so he avidly seeks the "know-how" to cope adequately with gynecologic problems.

On the other side of the coin, namely the side of the visiting lecturer, there is confusion regarding what topics the subject of office gynecology should embrace. It is, of course, easy for him to detail and expand upon the various presenting complaints and drop a few pearls regarding vaginitis, cervicitis, and the early detection of cancer. Unfortunately, I doubt that this will satisfy the doctor who attends the lecture – or the patient who subsequently consults that doctor. The subject seems to me to be much broader than this, because it is based upon the art of medicine and upon one of the most fundamental of human relationships, sex.

A basic point to remember is that women, by nature, and by training, are seldom direct in their approach to a gynecologic consultation. They may avoid telling the real reason why they are seeking treatment. Many years ago I was introduced to this principle by the wife of a college football coach in a neighboring town. She was 35 years of age and had 3 children. When the

youngest, a 10-year-old boy, was born, the patient's rectum was torn, and she never had bowel control thereafter. Examination confirmed the condition as described. In the consulting room later, the date was set for an operation and a hospital bed reserved. Something about the patient's attitude – I don't know what it was—prompted me to tell her that her condition was in no way connected with cancer and certainly would not lead to cancer. She registered considerable astonishment and then vigorously asserted that she didn't want to be operated on; she had changed her mind and was going home! Upon recovery from my astonishment at this unexpected announcement, I asked "Why?" "Oh," she said, "I can control my bowels fairly well, and the only reason I am here is that my friends told me this would lead to cancer. If it won't, I'm going home." And she did! Cancerphobia is so commonplace among gynecologic office patients that ever since that experience, whenever it is honestly possible to do so, I routinely tell the patient, "There is nothing even remotely suggestive of cancer in your story or physical findings." No matter how remote from the presenting complaint, the fear of cancer is so strongly implanted in the female mind that this statement is *never out of order.*

#### Hidden Motives for Seeking Treatment

Other than cancerphobia, conditions that impel women to seek gynecologic consultation include: marital infidelity, impending divorce, guilt feelings about reproductive inefficiency (miscarriage), guilt or fear that she may not be giving sexual satisfaction, and fear of pregnancy. The last, of course, is among the most common.

So many examples of fear of pregnancy come to mind. One was an attractive 32-year-old woman with a multitude of presenting complaints: headache, backache, bilateral low abdominal pain, and a profuse vaginal discharge. When I asked, "Do you wear a pad all the time, or even each day?" she hesitantly replied, "No." The pelvic organs were normal, and perhaps a small amount of discharge was visible in the vagina, but scarcely more than seen in many otherwise normal women. Sensing a hidden motive, I searched for it. She had been pregnant 3 times. The first resulted in an early spontaneous abortion with no fetus (she was curetted); the second, a normal girl, now 5 years old; the third, a hydrocephalic whose head at the current age of 3 years was 36 inches in circumference! It was so big, the child could not raise its head off the pillow. With two out of three of her attempts at reproduction resulting inefficiently, the patient was determined not to get pregnant again. I offered her sterilization, which she refused, then contraception, which she accepted. After several visits during the next few months, she was persuaded to put the hydrocephalic child into an institution and thus remove it from her daily consciousness. Not only were her symptoms ameliorated, but with her emotional outlook altered, the entire family profited. How quick, simple and efficient it would have been to treat the vaginitis! *To dig out the anxiety motivating the patient to seek treatment in cases such as this takes time, effort, and energy.*

I do not wish to imply that women manufacture pelvic complaints to gain

their ends. The process is subconscious, not volitional. Worry calls attention to a region previously neglected or magnifies existing discomfort or minor disease. Since woman's life is associated with reproduction, it is entirely understandable that the reproductive system often becomes the scapegoat.

At this point I wish to digress from the emotional aspects of "Office Gynecology" to talk briefly about the physical. Women seeking gynecologic consultation present a wide variety of symptoms: pain, bleeding, vaginal discharge, mass (palpable or visible abdominally or vaginally), urinary or fecal incontinence, or pruritus. To detail diagnosis and treatment of all of them would require a small book. On the other hand, it is entirely in order here to offer, in capsule form, some of the most important lessons I have learned during many years of gynecologic office practice.

**Some Practical Points**

- Most women who complain of pelvic pain have no demonstrable pelvic disease.
- Most women appearing in the office with a complaint of vaginal bleeding are pregnant, threatening to abort or have passed the fetus and now have retained placental tissue in the uterus.
- Leukorrhea originates below the internal os of the cervix, either as chronic cervicitis or vaginitis. Seldom, if ever, does it come from the uterine cavity, and virtually never from the fallopian tube. Differential diagnosis of the cause of vaginal discharge is advantageous both for the patient and the doctor.
- Since there is no cure for trichomonas vaginitis, give the woman palliative remedies she can use at home. In stubborn cases, examine the husband's prostatic secretion.
- Whenever yeast vaginitis is found, examine the urine and blood for possible diabetes mellitus.
- Beware recommending hysterectomy for pelvic pain when the only demonstrable abnormality is a small, nontender, readily palpable fibroid. Generally, one or several small nodules cause no symptoms, so removal of the nodules will not alleviate the pain.
- Examine the woman with a cystic ovarian mass more than once *(not* the same day). Better, ask a colleague if he can find it. Be reluctant to operate unless it is larger than a tennis ball and can always be palpated.
- Be careful in treating the woman with pruritus of the vagina. Virtually always she has been overtreated, often by herself, and sometimes the condition may be factitious.
- *Never* start treatment for cancer just on the basis of positive cytology. *Tissue biopsy* still remains the best and the *only positive* diagnosis for cancer.

Correct diagnosis in gynecology, as in all branches of medicine, is arrived at by an accurate history and a complete physical examination. Pelvic examination, it is true, remains one of the arts of medicine and so far has not yielded to precision-instrument diagnosis. Nevertheless, the master gynecologist makes the correct diagnosis just about the same way as anyone else: he listens to the story the patient tells him. When the pelvic findings and the history do not coincide, it is time to find out what *really* made the patient decide to come to consult you.

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# SURGERY

**L. Kraeer Ferguson, M.D.**
**University of Pennsylvania**

*L. Kraeer Ferguson is chairman of the Department of Surgery of the Graduate School of the University of Pennsylvania. He is also Professor Emeritus of Woman's Medical College of Pennsylvania and Consulting Surgeon at Philadelphia General Hospital and the U. S. Naval Hospital. He received his medical training at the University of Pennsylvania, Philadelphia, and at the University of Frankfort, Germany. Since then he has been a member of the faculty of the University of Pennsylvania. He is author of two textbooks,* SURGICAL NURSING *and* SURGERY OF THE AMBULATORY PATIENT, *and numerous papers, mostly on his special interest, abdominal surgery.*

## WHAT ARE THE FACTS ABOUT SURGERY FOR GASTRIC CANCER?

There is understandable pessimism among doctors in general about carcinoma of the stomach. The over-all results of surgical treatment of this disease have not been too good, and this may justify to some extent the smoldering reluctance to recommend surgery. On the other hand, surgical treatment is the only treatment that offers any hope of cure or even palliation; neither radiation nor chemotherapy has yet shown any substantial benefit.

But the case for surgical treatment of gastric cancer is not very compelling if it is based solely upon the arguments that surgical treatment is better than nothing and that desperate measures are justified in treatment of an incurable disease. Fortunately, recent experience, gathered from the literature and my own records, justifies a more hopeful attitude toward gastric cancer. And I think it strengthens the case for surgery.

But before discussing this experience, I would like to point out that the responsibility for diagnosing gastric cancer almost always rests with the physician in general practice. Clinics have tried (and so far failed) to develop reliable, practical screening procedures. For instance, a screening device developed at the University of Minnesota was based upon the fact that a majority of patients with carcinoma of the stomach are over 50 years of age and that 80% have achlorhydria. This method of screening proved impractical; in x-ray studies of 7,786 people over 50 years old with achlorhydria, only one in 357 had stomach cancer. So it seems likely that the best

detection clinic will remain the office of a general practitioner.

Unfortunately, detection is difficult, for cancer of the stomach is an insidious disease. The patient is unaware of its existence until complications result from its *size* (mass), from its *position* (difficulty in swallowing, as in cardiac carcinoma, or vomiting, as in carcinoma of the antrum), from *loss of blood* from its ulcerated surface (chronic anemia), or from its *interference with gastric secretion and motility* (chronic indigestion, loss of weight, or general deterioration in health).

### A Defense of Surgical Treatment

When presence of cancer is confirmed by x-ray and gastroscopy, you, as family physician, will want to discuss surgical treatment with your patient. Beyond the fact that there is little to offer the patient as an alternative, what hope can you give the patient when discussing surgical treatment of a disease which has such a poor prognosis?

Let us consider a few facts about surgery for gastric cancer and discuss some of the objections to surgery by answering a few questions about it.

*Isn't gastric cancer incurable? Why then should the surgeon accept the inevitable operative mortality when there is no hope of cure?*

Yes, the majority of patients with gastric cancer are incurable when first seen by the surgeon; however, a small but increasing proportion now can be cured. About two thirds of all patients referred to me have resectable tumors, and one quarter of these will live 5 years after surgery. In others for whom no cure is possible, worthwhile palliation can be achieved. Moreover operative mortality in our patients is only 7.9%, which is not great when one considers that, without surgery, it is a rare patient who lives more than one year after the tumor is diagnosed.

### Patients Who Should Receive Surgery

*Isn't it too late for surgery for patients who have had symptoms for longer than one year?*

You might expect that patients whose symptoms are of shorter duration would have the most favorable tumors for surgical treatment. Yet, Shahon at the University of Minnesota found that 60% of his patients who had survived 5 years after surgery had had symptoms for more than 6 months. In fact, 20% of his 5-year survivors had had symptoms for more than 2 years. This does not argue against the importance of early diagnosis and treatment, but it does mean that (1) the duration of symptoms does not necessarily indicate the extent of the disease; (2) the more malignant tumors grow rapidly, produce symptoms early, and have a less favorable prognosis; and (3) symptoms of long duration do not preclude the possibility of favorable surgical results. Actually the nature of the symptoms is more likely to have a bearing on the prognosis of the disease than its duration. McNeer found that 5-year survival after curative operations was 37.5% in patients with ulcer-like symptoms, 33.3% in patients with weakness and chronic anemia, and only 16.8% in patients with "chronic indigestion."

*Doesn't the size and position of the tumor affect operability? Would you say that a tumor large enough to be palpable is inoperable and incurable?*

No, the presence of a palpable mass does not preclude the possibility of resection or even cure, although the prognosis is less favorable when the tumor is large. Marshall of the Lahey Clinic found that 14.6% of the patients with a palpable resectable tumor survived 5 years or more. Also, surgery should be considered regardless of the position of the tumor, although there seems to be general agreement that lesions located in the distal stomach are most favorable for resection and cure.

*Aren't many patients with gastric cancer too old for surgery?*

Age is not really a compelling factor in the decision for or against surgery. On the contrary, gastric cancer seems to progress more slowly in the older patient, so that the possibility of resecting the tumor is usually better as age increases. On the other hand, the older patients are also less able to withstand the extensive operations that may be necessary for complete removal of the cancer, and, of course, the operative mortality is higher in the older age group.

Let me emphasize: without an exploratory laparotomy the possibility of cure is difficult to assess. Therefore, *surgery is indicated unless rare over-riding contraindications are present.* In our series, 93 of 94 patients received surgery.

### Prognosis After Surgery

*In your experience, what factors do bear on the possibility of cure of gastric carcinoma after subtotal gastrectomy?*

As you would expect, success depends primarily on the extent and rapidity of tumor growth. In our series of 93 patients, tumors proved resectable in 63 (68%). Almost 60% of all resected cases lived longer than 1 year; about 40% lived over 4 years; and 25.5% lived 5 years. Of the 42 patients whose surgery was considered curative (i.e., all visible tumor removed), 50% lived 2 years and 37% lived 5 years. As expected, best results were observed when the cancer was confined to the stomach. Sixty-one percent of those patients with no lymph-node involvement lived 5 years, compared to 22.7% of those with lymph-node involvement.

*You have discussed curative surgery. When removal of all visible tumor is impossible, do you consider palliative surgery for carcinoma of the stomach worthwhile?*

Of course the results would be expected to be better after curative operations; however, the proportion of patients whose lives will be extended and made more comfortable by palliative procedures is not negligible. In our series, the procedure was considered palliative in 21 of 63 patients whose tumor was resected. Thirty percent of these patients survived one year after palliative surgery. The operative mortality was 15.8%.

* * *

To sum up, there is nothing in our experience to justify an optimistic view of the prognosis of gastric cancer. The family physician will still dread the confirmation of suspected stomach cancer by the roentgenologist and gastroscopist. On the other hand, I believe that our experience does justify a more hopeful attitude toward surgical treatment.

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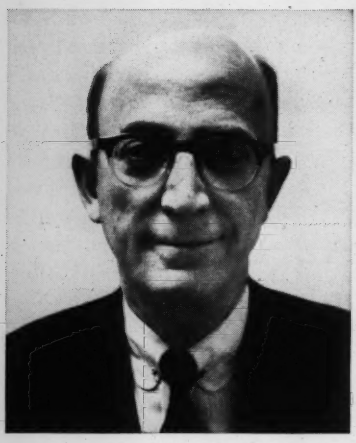
# INTERNAL MEDICINE



**Maxwell L. Gelfand, M.D.**
**New York University**

*Maxwell L. Gelfand is Associate Professor of Clinical Medicine at New York University Medical Center. He is associated with New York University, Knickerbocker, and Bellevue Hospitals, and serves as a consultant to the Meadowbrook Hospital. He is a Fellow of the American College of Physicians and of the New York Academy of Medicine, and a member of the New York and American Heart Associations. His investigative and clinical interest is focused mainly on cardiovascular disease and on physical diagnosis; on these subjects, he has published 35 articles and has presented several scientific exhibits at both national and local meetings.*

## DIAGNOSTIC CLUES LEARNED FROM LOOKING AT THE PATIENT

So many laboratory tests are available today that we are constantly being tempted to rely predominantly on quantitative measurements in arriving at a diagnosis. Patients, too, tend to regard numerical values as important. For example, we are daily confronted with the questions: "What is my cholesterol, Doctor?", "Shouldn't I have an electrocardiogram?", "What is Johnny's B.M.R.?", "How about a G.I. series?". These determinations are often helpful, but should only be used when indicated.

The history, so essential, is frequently hurried over because of the examiner's lack of time and patience. The great Osler often said "Listen to the patient; he is telling you the story!" How right he was! In addition, as the patient tells his story, we can learn much from his manner, appearance, speech, motions, and behavior.

Hippocrates, the father of medicine, was the greatest observer of all. Purely by external examination he classified body structure in its relation to disease entities in the phthisic, phlegmatic, choleric, and sanguine types. Cvostek, a famous Viennese clinician, was able to recognize many cardiac disorders by merely looking at the patient.

As the patient enters, we can learn a great deal by observing the gait. Hemi-

plegics drag the affected leg in a semicircle while walking and in addition keep the arm slightly flexed and still, as contrasted with the free and easy movements of the normal side. A tabetic has a slapping and flail-like gait, feet wide apart and eyes on the ground. Those with Parkinsonism walk with their head and body sharply inclined forward, usually with sharp, quick steps, appearing to be on the run. A typical spastic gait is usually seen in multiple sclerosis, amyotrophic lateral sclerosis, and in other nervous diseases involving lesions of the upper motor neuron. The scissors gait is usually noted in spastic paraplegics, and the ataxic gait in cerebellar disease, labyrinth disorders and Friedreich's ataxia. Astasia-abasia, described by Charcot, is an interesting condition in which hysterical people can neither walk nor stand in the erect position, but have perfect control of their legs while lying in bed.

### Capsule Collection of Clues

• Unequal pupils are not always pathognomonic of lues, for they are also seen in patients with chronic alcoholism, encephalitis, mesencephalic tumors, multiple sclerosis, extradural hematoma, diabetes, and Horner's syndrome.

• Increased pigmentation of the skin and mucous membranes occurs in Addison's disease, hemochromatosis, argyria, ochronosis, and Peutz-Jegher's syndrome.

• Gynecomastia, occasionally present in a normal male, is often observed in cirrhosis of the liver, eunuchoidism, malnutrition, Klinefelter's syndrome, digitalis toxicity and bronchogenic carcinoma.

• Clubbing of the fingers, so frequently associated with bronchiectasis, lung abscess, bronchogenic carcinoma, and subacute bacterial endocarditis may also be observed in ulcerative colitis, pulmonary arteriovenous fistula, cirrhosis of the liver, and Boeck's sarcoid. At times it is idiopathic. Unilateral clubbing may occur with a superior sulcus tumor, an innominate or subclavian artery aneurysm, or chronic dislocation of the shoulder.

### Clinical Conditions

Let us look at some clinical conditions which may be diagnosed by history and inspection. For example, a patient tells us that he is nervous, has lost weight despite a good appetite, cannot tolerate heat, and has marked weakness. On careful examination we find exophthalmus, a positive von Graefe sign, a tremor of the outstretched hands, moist palms, an enlarged thyroid gland, and restlessness. At once the diagnosis of hyperthyroidism leaps to mind. Similarly, hypothyroidism or myxedema can be just as easily detected by careful inspection of the patient whose symptoms are weakness, fatigue, hoarseness, and inability to tolerate cold weather. Skin pallor, absence of hair at the outer margins of the eyebrows, macroglossia, coarse dry hair on the scalp, and slow response to questioning round out the picture of this clinical entity.

Marfan's syndrome, a congenital connective tissue disorder, may also be easily suspected by a careful scrutiny of the patient. A long, slender body-build, with the distance between the hips and lower extremities twice that from the shoulder to the hips, long, tapered fingers, and either a pigeon breast or kyphoscoliosis

suggest its presence. Other features are then sought to confirm its existence.

Paget's disease once seen can hardly be forgotten. The typical bowing of the legs, dorsal kyphosis, and enlarged calvarium, together with the patient's report that his hat size has recently become larger, fit no other entity. Similarly, acromegaly with its characteristic facial features, i.e., prognathism, enormous enlargement of the hands, feet, and forearms can easily be recognized by inspection.

Peutz-Jegher's syndrome is characterized by a history of familial gastrointestinal bleeding plus the presence of tiny, dark-brown or black macules around the facial orifices and on the oral mucosa.

These are but a few of the many diseases that can almost be diagnosed by inspection alone. In addition, there are some clinical entities in which two conditions co-exist; one, overtly, easily recognized by inspection, and the other cryptic, to be sought after. Thus, the presence of neurofibromatosis should arouse suspicion of a pheochromocytoma, for at times the two may be present in one patient. A migratory phlebitis may indicate an underlying neoplasm either in the lung, pancreas, ovary, or gastrointestinal tract. Patients with dermatomyositis often have an underlying malignancy, and those with mycosis fungoides occasionally conceal a lymphoma or Hodgkin's disease. Acanthosis nigricans in young people is often associated with a neoplasm of the stomach, whereas herpes zoster in the aged may at times indicate leukemia or lymphoma. Polydactylism, observed externally, should alert us to the possible existence of an internal genetic defect.

The instances which have been described show how much valuable information can be obtained merely by careful inspection of the patient. A thorough external examination can furnish vital clues to the diagnosis of these and many other clinical entities. Truly, if we "look at the patient," the diagnosis may well be apparent.

Next month in CONSULTANT:

When Your Patient Should Stop Driving—a helpful article by Harold Brandaleone, M.D., of the AMA's Committee on Medical Aspects of Crash Injuries and Deaths.

How to Perform Closed-Chest Cardiac Massage—an illustrated how-to-do-it article by James R. Jude, M.D., showing the new Johns Hopkins technique for reviving hearts "too good to die."

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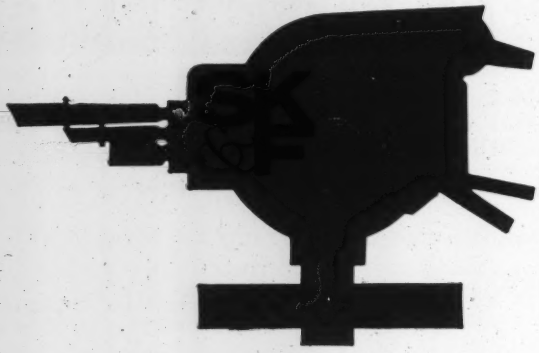

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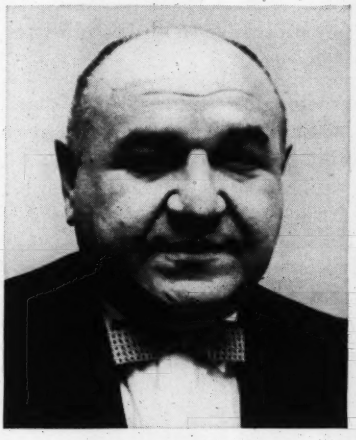
# PSYCHIATRY



**Maurice E. Linden, M.D.**
**Department of Public Health, Philadelphia**

*Maurice E. Linden is Director of the Mental Health Division of Philadelphia's Department of Public Health, and Assistant Professor of Psychiatry at the University of Pennsylvania School of Medicine. In addition to his private practice, he serves as psychiatric consultant for Philadelphia's Mercy-Douglass Hospital and the Norristown (Pa.) State Hospital. He is president of the American Group Psychotherapy Association (1960-1962), and has authored over 85 papers for medical journals and textbooks. He is especially interested in promoting mental health through preventive psychiatry.*

## WHAT PRINCIPLES OF MENTAL HEALTH CAN BE TAUGHT TO PARENTS?

Throughout much of the last half century, parents have been confronted with so much advice about child-rearing that many of them no longer rely on historical knowledge, common sense, and confidence in their own ability that parents used to use to guide themselves, however shakily, in rearing children. Certainly much of the advice has been good. But some of it has been unbalanced and some downright harmful to the psychological well-being of children.

It is not possible to cover here all the factors that contribute to emotional disturbances of children and adolescents. There are some habitual attitudes within families, nevertheless, that are pretty reliable producers of trouble and that can be highlighted. Absence of genuine love among members of a family is an unfortunately common one. Of course, love can be neither taught nor legislated. It often needs to be emancipated from neurotic bondage — a difficult task. Failure to apply common sense is another important factor. Sometimes common sense is eclipsed by emotional problems; sometimes it is stifled in favor of viewpoints offered from external sources.

An article such as this, of course, runs the risk of doing the very thing that should be avoided. Still I believe that there are fundamental principles of love and common sense that physicians can teach to parents and prospective parents who seek help in rearing their children.

The alternative to suggesting such principles to the naive is to allow the children to grow up with problems in character formation such as chronic lack of trust, disrespect for authority, feelings of inadequacy, a profound sense of guilt, incapacity to compete normally with others or an enduring, deep feeling of terror or impending doom. There is little doubt now that the greater the appropriate leadership and good example-setting on the part of parents, with an affectionate appreciation of the child's potentials, the more secure and well integrated the child's ultimate personality will be.

### Some of These Principles May Be Stated in Short Maxims

- Do prepare children for extraordinary coming events such as the birth of siblings, surgical operations, moving to another home, and so forth.

- Do not expect or depend solely on social agencies, doctors, or ministers to solve the ordinary problems of child-rearing. Responsibility for solving problems of growth and development cannot be delegated; it rests ultimately with the parents.

- Do strengthen spiritual values, but reduce to a minimum their being dependent upon fear of reprisal.

- Do not try to remove from the environment all things such as comic books, horror stories, etc., that are out of harmony with our best intentions. (It is not possible. Instead strengthen the child's ability to make good choices.)

- Do not let leadership of the family default to the mother only.

- Do not stifle all aggressive drives in children.

- Do not substitute rigid discipline for *understanding.*

- Never threaten children with mutilation or bodily harm as punishment or discipline, or even "for fun."

### Others Require More Explanation

Other rules of child-rearing, especially those that relate to sex, merit a bit more explanation. These are important because many parents seem to be confused by trying to apply psychological theories they have read (particularly about matters of sexuality relating to children) rather than relying on common sense.

- Make sure that children do not witness sexual relations among grownups—as they might, accidentally, during the course of their night wanderings. A child is both excitable and stimulatable, but he doesn't have the anatomical devices or social sanctions for the appropriate release of such energies. A sexual scene to a child is both thrilling and fearsome. A great deal of non-specific energy becomes pent up in the child and may give rise to berserk behavior accompanied by the neurotic need to suppress a guilty secret.

- Avoid all forms of seduction — the direct sexual kind, of course, but also the indirect wheedling or cajoling kind. Sexual seduction interferes with the child's normal emotional development. The indirect form perpetuates infantile modes of behavior that are based not upon human relationships but rather upon the implication of rewards and various

forms of bribery. The latter may lead to dependency, "spoiled" behavior, irrationality, covetousness and overmaterialism.

• Do not overdo or underdo toilet training. Find a middle road between leniency and strictness, between indifference and over-emotionalism, and between beginning too early or too late. Important elements of character are laid down in the toilet training experience: a sense of values, prudence, reliability, altruism, stability and dependability. Excessiveness in toilet training in any direction may produce analogous excesses in character formation.

• Answer children's sex questions but do not over-answer them. Wholesome attitudes toward sex and love require that a child's natural curiosity in such matters be satisfied in keeping with his needs, his level of understanding and the actual motive for his inquisitiveness. The answer to a sex question should not be too complete. Some degree of unsatisfied sexual curiosity contributes to continuing general interest, the spirit of inquiry and scholarliness in the course of growing up.

My own experience strongly suggests that most parents know the bulk of these rules already, but many have traded their confidence in them for allegedly authoritative advice which is all too often inconsistent. The family physician is in an excellent position to restore to parents some confidence in their own common sense and in their natural inclinations as parents, and to teach common sense to those unaware of their own considerable potential to be good parents.

## *QUESTIONS AND ANSWERS*

Q. *Your points may be well and good when parents ask how to handle certain problems of rearing their children. But what about parents who do not ask, and yet are clearly making mistakes, such as being too strict with their children, or jokingly threatening them with bodily harm?*

A. Sometimes I'm asked whether the physician has the moral right to try to correct parents in their method of handling children. I think that just as we physicians ask questions in examining for physical disorders, we can and should inquire into factors that contribute to mental unhealthiness. If the parent does not bring up the subject, you can turn the conversation toward it. Take, for example, the parents who

are clearly stifling all aggression in their child. An indirect approach might be to ask whether the child is difficult to handle. This will usually lead to a discussion of how the parent feels about aggression in his child, and permits you to give necessary advice. Then, there is the broadside approach: talking about some typical problems parents have with children, and commenting, "I've noticed the very same thing in your child." Most parents are eager to discuss their problems of parenthood. If you feel they are clearly making mistakes, you should create an opportunity for them to ask your advice.

Q. *I realize that parents should not stifle all aggressive drives in children, but how would you suggest getting this point across to parents?*

A. In discussing this point with parents, I use a simple analogy, saying that the aggressive drive in children is like a balloon. You can press on part of it and if you do, the air inside must go somewhere, and will push out the other side. If you press both sides hard enough, the balloon will break. Likewise, you can suppress some aggression in children (we obviously must suppress destructiveness and inhibit dangerous acts) but the aggressiveness is still there. If you were to suppress it entirely, the child's spirit would eventually break. Aggression should be channeled into acceptable areas—games, sports, scholastic competition, and achieving mature behavior. Here are some specific things I tell parents: Don't take away all toys that the child may use to strike things with. Do encourage children to be victorious – they must win sometimes, even over adults. Don't treat the child who talks back as if he's committed a crime; instead, try to find out what he's really saying. The parent can see from these examples that there are many ways aggression can be expressed. If he understands aggression and accepts it as normal, he'll relax and the child can develop more healthily.

Q. *Don't you sometimes feel that in order to help the children it would be necessary to completely re-make the parents? Some of your points (such as not assigning the leadership of the family to only the mother) seem difficult to realize.*

A. It's true that some parents have deep-seated problems that interfere with their rearing of children. But, in a great many cases, calling the parent's attention to what may happen may help prevent it. I recently saw a mother who was trying to toilet-train her 4-month-old son, because she had heard that early toilet training would help children mature faster. This kind of situation can easily be corrected by educating the parents, and so can most of the principles I've outlined. There aren't any panaceas, of course, just as aspirin doesn't cure all headaches. In our experience, though, discussion and advice can help correct many situations in child-rearing which are unwholesome.

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# NUTRITION

**Jean Mayer, Ph.D., Harvard University**

*Jean Mayer is a consultant in nutrition at the Children's Hospital Medical Center in Boston and since 1950 has been an Associate Professor of Nutrition at the Harvard University School of Public Health. He has served the United Nations as a member of the Nutrition Division of the Food and Agriculture Organization, as a consultant on social and health affairs, and as a member of the Committee on Caloric Requirements and the Committee on Protein Requirements of the World Health Organization and the Food and Agriculture Organization. Currently, he is a member of the Editorial Board of the* AMERICAN JOURNAL OF PHYSIOLOGY *and a member of the Editorial Advisory Board of* POSTGRADUATE MEDICINE. *His contributions to the literature (200 articles for scientific publications and 25 for lay publications) have covered many aspects of experimental and clinical nutrition, particularly the physiology and biochemistry of obesity.*

## OBESITY IN ADOLESCENTS

Obesity in adolescents differs in several ways from that in other age groups — in ways that make treatment a special problem. At no time in life is a diagnosis based on height-weight charts more precarious; differences in rates of linear growth, in muscular development, in rates of sexual maturation introduce variables not present in younger children or in adults. Commonly, both boys and girls have an appreciable increase in subcutaneous fat just before puberty. Boys then tend to actually thin out while their height shoots up. Girls, on the other hand, tend to keep their fat while their height increases, so that there is *relative,* rather than absolute, thinning (the actual thinning process, if it occurs, takes place much later, in the late teens). Only when this deposition of puppy fat becomes clearly excessive or too persistent does it constitute a medical problem. This happens in about 15-20% of all adolescents, at least in the Boston area.

Because of individual variations in build and relative growth — and because of the normal evolution of body fat content — the only reliable criterion of obesity in adolescence (short of actual determination of body fat by soft-tissue X-ray or densimetry) is experienced clinical observation, supplemented if necessary by pinching with or without calipers. Similarly, the best guide for deciding how much a given adolescent should weigh is not height-weight charts but, rather, serial inspections during the

period of weight loss.

### Attitude of the Physician

We must remember that obesity is not a moral issue, but a medical problem, complex and as yet ill-understood. Appetite is still a largely unknown mechanism involving metabolic, gastric, hypothalamic, and cortical factors; it can be disturbed by many physiological and psychological factors which may have nothing in common except the creation of a positive energy balance. To equate obesity with gluttony and treat the adolescent patient with an inspirational talk and a diet sheet not only lays the groundwork for quick failure, it may actually harm the youngster by reinforcing feelings of guilt already induced by a censorious environment, and by causing further withdrawal into lack of social contacts, physical inactivity, and overeating. We must remember at all times that no group is more uncertain about their own body and more easily thrown into feelings of guilt and into concealed depression than adolescents.

### Using Hereditary Data

We know that obesity runs in families, involving genetic as well as environmental factors. Studies in Massachusetts high schools have shown that less than 10% of the children of parents of normal weight are obese, but the proportion rises to 40% if one parent is obese and to 80% if both parents are obese. Studies of identical and fraternal twins, some of whom were raised in different households, have shown that food habits are not the only factors involved. Instead of denying the facts of heredity, it is more important and useful to use them to *locate* obese youngsters, to confirm a diagnosis (and a possible prognosis) and, more important, to try to prevent the development of obesity in susceptible children and adolescents. Obesity is most malignant when onset is early.

### How Important Is Exercise?

Probably no single factor is more frequently responsible for development of obesity in adolescents than *lack of physical exercise.* The value of exercise in weight control has been obscured by misconceptions, by four erroneous attitudes: (1) the overwhelming emphasis on caloric *intake* to the almost total exclusion of consideration of *output;* (2) general underestimation of the caloric cost of exercise; (3) the erroneous belief that increase in physical activity is always followed by an increase in appetite; (4) forgetting that the kinds of participation, recognition, and success that adolescents enjoy, and the confidence which these bring, can be achieved only by activities that entail physical exercise. We should remember that caloric output is determined as much by *energy balance* as by caloric intake. The range of daily caloric output in adolescent boys may go from 2800 calories for extremely inactive youngsters to over 6000 for athletic young men engaged in strenuous sports. The caloric output per hour in many typical teen-age activities is surprisingly high. Here are some typical values, calculated for a 150-pound subject:

| Activity | Caloric Output/Hour |
|---|---|
| walking (3 mph) | 270 |
| walking (4 mph) | 350 |
| running | 800-1000 |
| dancing | 200-400 |
| golfing | 300 |
| skiing | 600-700 |
| tennis | 400-500 |

Recent evidence obtained in experimental animals, in adult men and women, and especially in adolescents shows that voluntary food intake does not necessarily increase with activity. If an individual is already reasonably active, additional hours of daily exercise *will* increase his food intake. On the other hand, there is a wide sedentary zone where increasing exercise from very low levels of activity to somewhat higher levels does *not* increase appetite. In other words, if adolescents spend most of their waking time sitting, then adding an hour or two of activity to their schedule does not increase food intake.

Repeated studies have shown that the great majority of obese adolescents eat less than average non-obese adolescents of the same sex. The laws of thermodynamics are not flouted by this paradox, however; the inactivity of the obese adolescent easily accounts for the calories which permit excessive fat deposition. We have shown that in such individuals, stepping up exercise even without paying much attention to diet invariably results in weight loss. Thus, if there is any basic rule in managing obese adolescents, chances are it would be *to increase their physical activity.*

### Diets

It goes without saying that, in considering diets for adolescents, the first concern should be nutritional adequacy and balance. No age group is more subject to fads; as a result, their diet is often unbalanced and sometimes frankly deficient—particularly if they are trying to lose weight. At the Adolescent Clinic of the Children's Medical Center in Boston, we have seen many adolescent girls who had put themselves on a reducing diet so low in protein and iron that it resulted in anemia (incidentally, this is a major cause of anemia in girls in this age group). Avoiding whole classes of foods because of misconceptions about their effects on skin appearance and weight is common. The physician can combat these problems by making sure adolescent patients have sound basic knowledge of the caloric and nutrient content of common foods. Without such knowledge, no reduction regimen can succeed in the long run.

The major problem with diets is that they tend to fail because they leave the patient feeling too hungry. A solution to this problem—one that works especially well for adolescents – is to *put the patient on smaller and more frequent meals,* rather than three meals a day without snacks. The fact that most of the overeating is often done in the evening hours and at night may make it expedient to actually legislate the size of the after-dinner snack, rather than prohibit it altogether. Telling the patient he can have a glass of orange juice when he is out with his friends, for example, is more effective than telling him he cannot eat sundaes or anything at all.

Diets for adolescents should be individualized, adapted to the rate of growth and development and the energy expenditure. As in other age groups, weight loss should be slow to avoid excessive fatigue; this is especially important for adolescents because they are already prone to hypochondriacal concerns. Ideally, if the patient is still growing and not too obese, he should have a caloric

intake which will allow him to grow up to the ideal height for his present weight. If additional loss is desired, it should not proceed at a rate faster than a pound a week (which corresponds to a deficit of 500 calories per day).

### Emotional Aspects

Not infrequently, overeating may be due to psychogenic factors. If grief, lack of affection or success, or of popularity are involved, harm may be done by superimposing the discomfort of food restrictions to an already difficult situation. In such cases, food deprivation may make emotional difficulties even worse. A better solution, when it is feasible, may well be increasing the patient's energy output, by increasing his activities.

Our society, consciously or unconsciously, is becoming more and more punitive about the obese person. We have some evidence, for example, that there is some discrimination in college admissions toward obese youngsters. Even well-meaning parents, teachers, and classmates may be the cause of additional difficulties. Further harm must not be done by the physician in this regard. It is all too easy to encourage a sense of inadequacy in the adolescent. The fact that on a statistical basis our success in permanent weight reduction is low should incite us to humility rather than to passing the blame on to our young obese patients.

# GASTROENTEROLOGY

**J. Alfred Rider, M.D., Ph. D.**
**University of California**

*J. Alfred Rider received his medical degree and Ph.D. at the University of Chicago School of Medicine. Certified in Internal Medicine in 1952 and in Gastroenterology in 1954, he is now Assistant Clinical Professor of Medicine at the University of California School of Medicine in San Francisco. He is a Fellow in the American College of Physicians and a Fellow in the American Gastroenterological Association. His professional affiliations include the American Gastroenterological Association, the American Society for Pharmacology and Experimental Research, and the American Gastroscopic Society. He served as one of the two editors of the book* DISTURBANCES IN GASTROINTESTINAL MOTILITY, *and is author of numerous papers on original research in gastroenterology disorders. In addition, he is a contributor to* ENCYCLOPAEDIA BRITANNICA.

## DUODENAL ULCER: WHY DOES TREATMENT OFTEN FAIL?

Duodenal ulcer rarely presents a diagnostic problem because its symptoms are so well known and roentgenologic facilities are so readily available. Nevertheless, it remains a disease of major importance not only because of its high incidence (approximately 10% of Americans at some time in their lifetime have a duodenal ulcer) but also because there are still too many unnecessary therapeutic failures and recurrences.

Why do these failures occur? There are three main reasons, I believe. At the risk of controversy, I would like to discuss them—and suggest alternative methods of treatment that have proven practical for me. The first stems from the *common misconception that diet regulation alone is sufficient management.* Of course, from a common-sense standpoint the ulcer patient should avoid spices, gas-forming foods and other irritants in the diet. Since coffee, chewing gum and tobacco may stimulate gastric secretion, their use should also be restricted and, if possible, discontinued. Except in the very acute cases, however, strict control of diet actually plays a minor role in therapy. Furthermore many patients have a reluctance to accept it. I have seen exacerbation of symptoms in numerous patients who, after struggling with strenuous long-term diets, finally

rebelled against the entire treatment and ended up with no regimen at all, to their obvious detriment.

A second reason for treatment failure is *improper use of anticholinergic and antisecretory drugs.* The rationale for curtailing acid secretion is a sound one, for it is based on laboratory and clinical knowledge of peptic ulceration. Of course, the primary cause of duodenal ulcer is not known, and all we can say with certainty is that the ulcer is the end result of a pathological process in which the gastroduodenal mucosa fails to withstand the digestive action of acid gastric juice. Surely, then, gastric acid is an indispensable factor in the formation of duodenal ulcer. When gastric acidity is effectively and completely neutralized or abolished, as by therapeutic irradiation of the gastric mucosa, a duodenal ulcer will heal and remain healed as long as the acid is completely neutralized or absent. In short, I have never seen the dictum "no acid, no ulcer" refuted.

### Why Anticholinergics Fail

If the benefits of controlling acid secretion are so widely recognized, why do anticholinergics and antisecretory agents sometimes fail? Usually, I have found this is because the agents were not sufficiently individualized: the dose is inadequate or it has not been given long enough.

Underdosage seems to occur exceptionally often with anticholinergic drugs. These drugs, widely used since they were introduced 10 years ago, selectively inhibit the parasympathetic ganglia and/or the terminal nerve endings (or act on the parietal cells themselves to decrease or abolish gastric acid production). Ideally, the drug we choose should be capable of both achieving and maintaining inhibition of gastric secretion. There are a number that will do this, but to succeed they must be used in the dose that is effective not in the "average" patient, but in the person being treated. Also, no anticholinergic will be equally effective in all persons; sometimes a patient will respond much more favorably to one than to another. Thus, both the dosage and the drug must be individualized.

### Testing a Drug's Effectiveness

Usually the average recommended dose is used but if the clinical results are not good then one must use a different method. Thus, when greater accuracy is needed, as in the chronic patient, one can test the effectiveness of an anticholinergic agent quite simply in the following manner. A Rehfuss tube is passed into the stomach, and a one-hour, fasting, basal gastric collection is obtained. The gastric juice is titrated in order to determine the amount of free acid present. A solution of antisecretory drug is then instilled through the tube into the stomach and the tube is clamped off. One hour later, after the drug has passed into the small intestine and after absorption has begun, continual gastric aspiration is resumed. One can then determine quite accurately how such gastric acidity has decreased and whether anacidity has occurred. The duration of effectiveness of the drug can also be determined in this way. By using the results of objective tests such as this, it is possible to individualize, to a high degree, the dosage of antisecretory drugs.

### Proper Use of Antacids

A third—and equally important—reason for treatment failure occurs with improper use of *antacids,* the sheet anchor of duodenal ulcer therapy. Many drugs such as calcium carbonate, combinations of aluminum hydroxide and magnesium compounds, or dihydroxy aluminum aminoacetate will neutralize stomach acidity. But all too often they are not given in amounts large enough to be effective, and underdosage is as much the rule as it is the exception. It is usually necessary to give 1 to 2 Gm. of antacid, in each dose.

In addition, studies in our laboratory have shown, as one might expect from the known emptying time of the stomach, that only rarely does an antacid neutralize stomach acid for longer than half an hour to 45 minutes. Therefore, to provide the necessary environment for healing, the patient should, at least during the first week or two of therapy, take an antacid every half hour or every hour during the day. For some, several doses are necessary at night. (Four ounces of milk, a dietary item most patients will accept, can also be used effectively to neutralize gastric acidity and can be alternated with other antacids for variety.) Beginning the second week and continuing for approximately 2 to 3 weeks, the antacid may be taken every 2 hours.

### Prolong Treatment with Antacids

After approximately one month of this regimen, medication may be taken in the mid-morning, mid-afternoon, an hour after supper, and at bedtime. This program should be continued for at least 3 to 6 months in patients with early acute ulcers and in patients who do not secrete a large amount of acid. However, in those who secrete a large amount of acid and/or give a history of recurrences, I feel quite strongly that antacids must be taken for several years or until the patient's life is stabilized. Once he has regular hours and regular habits so that he is relatively free from emotional stress and strain, the antacid can be omitted. But treatment should be resumed whenever stress recurs.

By the way, some patients during this therapy develop constipation and require a laxative; magnesium carbonate (1-4 Gm. daily) is excellent for this purpose, since it is an antacid, too.

To summarize, I would like to repeat that probably the most important measure in managing duodenal ulcer, and preventing recurrence, is to provide *adequate* and *prolonged* control or neutralization of gastric juice. In general, the drugs which do this are as safe as they are effective. Under such therapeutic circumstances, there is little to lose if treatment is vigorous, but much to be lost if it is inadequate.

## QUESTIONS AND ANSWERS

Q. *Don't emotional factors account for much of the difficulty in treating duodenal ulcer?*

A. Yes, as we all know, emotional stress, tension, strain, worry, and other psychic difficulties may precipitate—and perpetuate—duodenal ulcer. We can make the patient aware of these factors and, as a result of this awareness, he may be able to modify or even to eliminate some of them. But mild sedation is useful because it may decrease psychic stimulation and thereby reduce psychically-stimulated gastric secretion. Some patients respond well to barbiturates, meprobamate, or other tranquilizers. But usually it is impossible for anyone to avoid all or even a significant portion of the circumstances in his life that may cause tension especially if he is to be gainfully employed. In fact, his tensions may not be abnormal; only his reaction to them—the ulcer—can be considered so. It is not generally possible to use medication to completely eliminate tension over long periods of time. For this reason, the more specific measures such as anticholinergics and antacids are all the more important.

Q. *Does the occurrence of side effects with anticholinergics indicate that the medication is causing an adequate reduction of gastric secretion?*

A. No. The rule of thumb method for using anticholinergics indicates only that the patient is receiving all he can comfortably take, not that the dose is adequate. Even gastric secretion values obtained in a fasting stomach are not necessarily indicative of the amounts of acid that may be secreted when the patient is eating. This is one of the reasons antacid therapy is so important, for we do know that given in the doses and in the frequency recommended, adequate control of acidity is usually achieved.

Q. *Are you saying that dietary control alone can never succeed in healing a duodenal ulcer?*

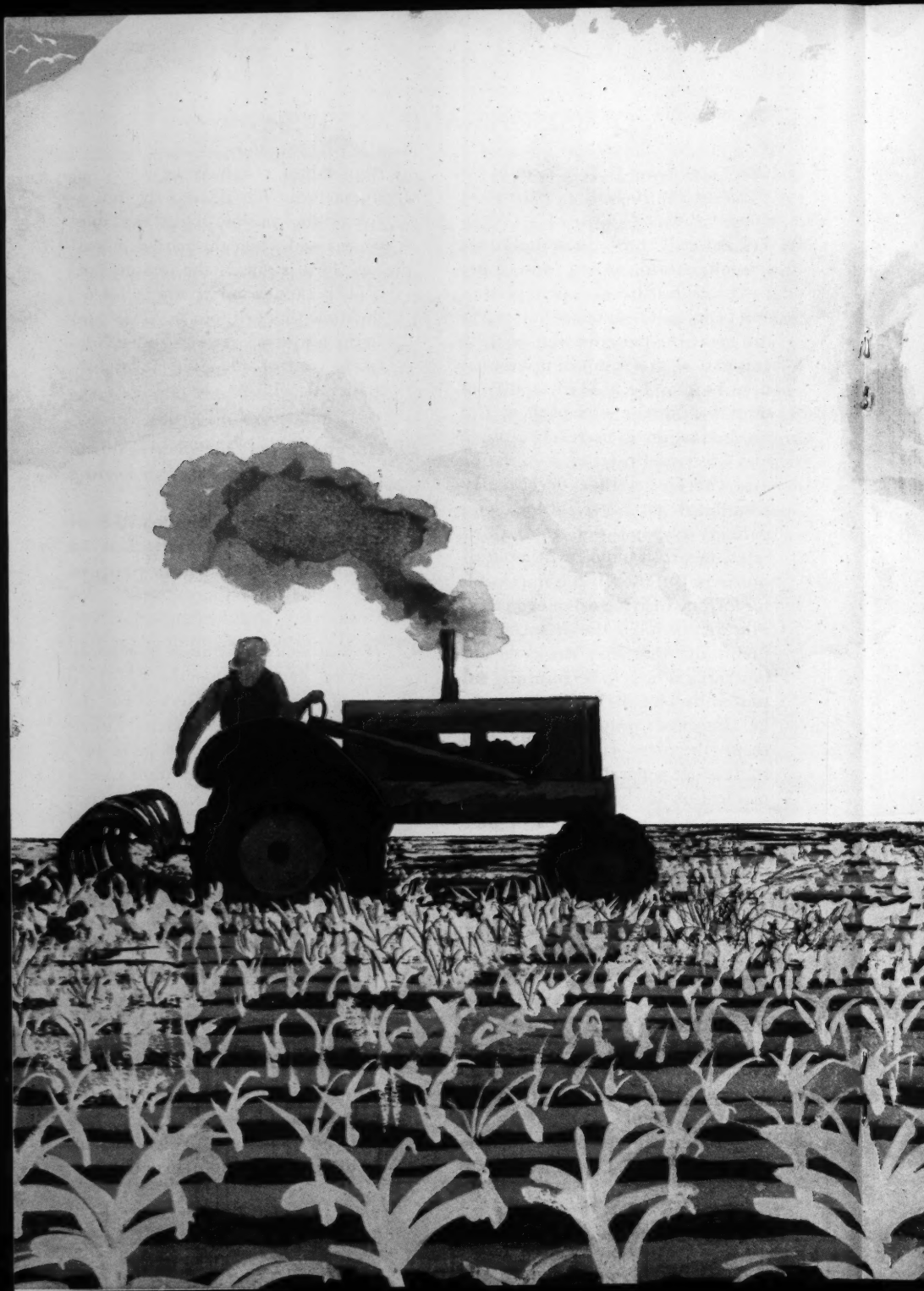
A. No, because many ulcers will heal without any treatment. But in chronic or recurrent ulcer patients, diet is of little importance.

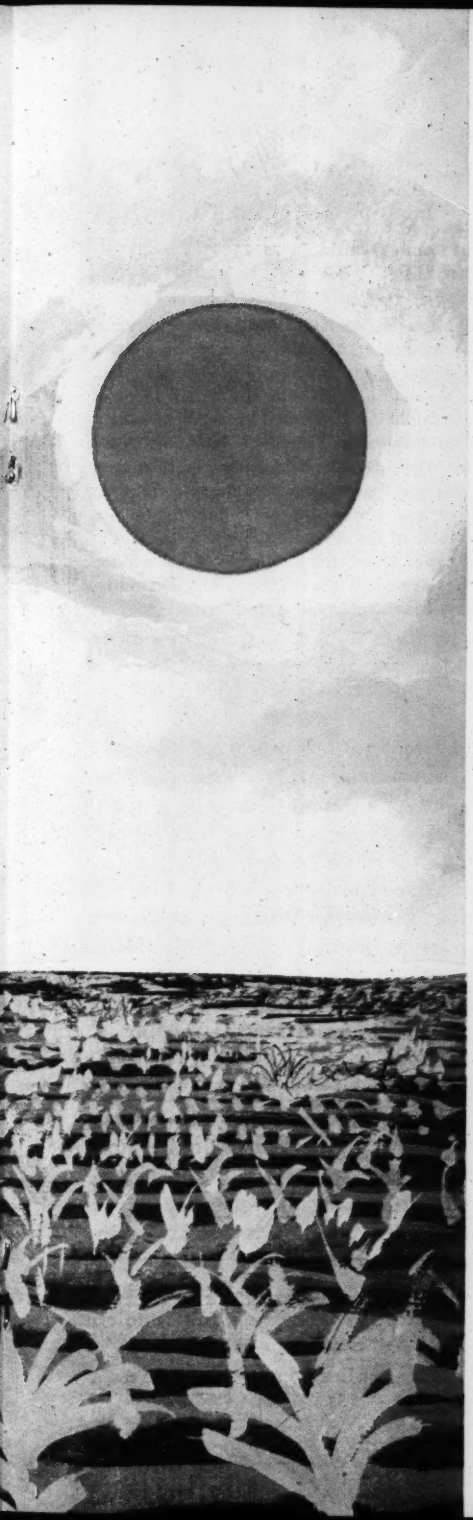
Q. *How often do you find surgery necessary for duodenal ulcer?*

A. Surgery should be reserved for the complications of duodenal ulcer such as massive hemorrhage or perforation. The truly resistant case is rare. In any case, surgery is not necessary in more than 5-10% of all patients.

Q. *There has recently been some evidence that when given hourly, certain popular antacids cause an excessive intake of sodium for patients with heart disease or cirrhosis. Is this problem so rare that it is only of academic interest, or do you consider it a frequent problem?*

A. In my experience this is not a frequent problem, especially since I do not find it necessary to give antacids hourly for more than several weeks.





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# DERMATOLOGY

**Milton M. Cahn, M.D.**
**University of Pennsylvania**

*Milton M. Cahn is an Assistant Professor of Dermatology at the School of Medicine and the Graduate School of Medicine of the University of Pennsylvania. He is also an Associate at the Albert Einstein Medical Center in Philadelphia. He received his medical education at Temple University School of Medicine. After service during World War II, he spent several years in general practice and then took postgraduate training in dermatology at the University of Pennsylvania. Dr. Cahn, a Diplomate of the American Board of Dermatology, has had about 40 articles published to date. Many of these articles dealt with his work in photosensitivity, one of his favorite research subjects.*

## OINTMENTS AND RELATED TOPICALS: A FEW FACTS AND FANCIES

Recently I was asked to see a woman whose treatment with hydrocortisone in *ointment* form caused a marked worsening of the macerated moist erythematous eruption between her breasts and under her arms. Simply changing treatment to plain tepid water compresses and hydrocortisone in *lotion* form brought the eruption under control within a few days. Then, in place of it, the patient used a bland powder (equal parts of talc and zinc oxide) to keep the healed areas free of moisture and to reduce friction between opposing skin surfaces. In treating common skin disorders, as in the case just cited, prescribing the wrong drug *form* can often add to the patient's miseries. What works so well in a lotion base may not work at all in an ointment; in fact, it may aggravate. Many of the pitfalls here can be avoided by keeping in mind a few simple points.

### Ointments, Creams

Ointments and creams should be used in dry, chronic dermatoses only. They have the capacity to soften and penetrate the skin, entering the follicular orifices readily. They promote healing by laying down an occlusive film that impedes evaporation at the skin surface treated. Even chronic, heavily-scaling indolent plaques of psoriasis may respond to repeated application of plain petrola-

tum; in such cases the incorporation of crude coal tar (3-10%) is helpful.

The main function of ointments and creams, therefore, is to lubricate and protect the skin, and to transport into it any incorporated medicaments. Because of their occlusive and macerating properties, they should not be used on moist or oozing dermatoses nor on intertriginous areas, such as the axillae, groin, or skin folds in the obese. Some ointments and creams, especially those of the tacky, greasy variety, can cause folliculitis if applied to hairy areas other than the scalp. The newer, water-miscible ointment and cream bases [such as hydrophilic petrolatum and hydrophilic ointment (U.S.P.)], however, are much less likely to present this problem.

### Pastes

Pastes act by absorption to remove minimal exudates and are mainly used in treating subacute lesions that tend to crust, vesiculate, or ooze. They form a non-occlusive, protective covering for the skin and permit normal water loss by evaporation. Lassar's paste is the notable example of a paste and consists of 25% starch, 25% zinc oxide, in petrolatum q.s. A prescription I frequently use is the so-called "1-2-3 paste," which consists of Burow's solution 10 cc., hydrophilic petrolatum 20 Gm., and Lassar's paste 30 Gm. Care should be taken to remove pastes gently and not to irritate the underlying skin surfaces further. Use of mineral oil, Spry, or Crisco will make the job easier.

### Lotions

Lotions are indicated chiefly for subacute, "less angry" dermatoses where a drying effect is wanted. These liquids contain solids suspended or dissolved in alcohol, water, or mixtures of the two, or other organic solvents. They are easy to apply and allow secretions and exudates to pass fairly well, but with overuse lay down a heavy coating that may lead to increased inflammation. Calamine lotion is a simple but effective shake lotion. Another simple one is zinc oxide, talc āā 20%; glycerin 15%; and water q.s. Shake lotions should not be used where there is a lot of hair. Some of the newer water-miscible lotions, especially those with hydrocortisone or other steroids, are easily applied and do not cake, so they can be used over larger body areas than the older formulas that were so difficult to remove.

### Compresses, Soaks, Baths

Compresses, soaks, and baths provide a drying and decongestion of tissues by means of evaporation. They are the only local applications that should be used for acute, swollen, angry, red, vesiculating, and oozing dermatoses, no matter what the cause. Under no circumstances should ointments or creams be used.

Of the three measures, compresses provide the greatest evaporation. They may be soaked in any number of lukewarm solutions, partly wrung out, and used at room temperature. Solutions commonly used include 1:40 aqueous Burow's solution, normal saline (2 teaspoons of salt to quart of water), milk, or potassium permanganate in proper dilution. For example, potassium permanganate for the bath is prepared in a very dilute solution (1:50,000) made by thoroughly dissolving 20 Gr. in a half tub (20 gal.) of water. For other local compresses, this solution is made less dilutely with a ratio of 1:15,000.

The simplicity and usefulness of compresses is illustrated in a woman with what presumably was "soap" or "detergent" dermatitis and characterized by an acutely inflamed, vesicular eruption of the fingers and backs of both hands. She was advised to apply tepid Burow's solution (1:40 dilution) compresses, one hour "on" and one hour "off" for the first day. By the second day, the marked exudation had decreased so she applied the compresses for 30 minutes out of every 2 hours and, at night, a "1-2-3" paste. During the subacute phase, she was instructed to use a proprietary hydrocortisone lotion sparingly 3 times a day to reduce inflammation and promote drying. Compresses were used less frequently although the "1-2-3" paste was continued. At this point, the patient now complained of excessive dryness and so a lubricating ointment (equal parts of hydrophilic petrolatum U.S.P. and water) was prescribed.

Soaks and baths containing hydrolyzed starch (Linit or Argo) or colloidal oatmeal are used when fairly large skin areas are afflicted. Sometimes, though, plain water will do, as in the case of a young man with a poison ivy dermatitis. He had developed a typical exudative vesicular eruption over his face and hands with a rapid generalized dissemination of the rash over most of his body. He used compresses on his face, but because of the large body area involved, took tepid baths; otherwise treatment was similar to the case just mentioned.

As the acute and exudative phase subsides, wet dressings, soaks, and baths should be decreased in both frequency and duration of application, otherwise, as in the woman with "soap" dermatitis, they will become overly drying and irritating in action. And as in her case, a paste can be used in place of nightly compresses or soaks, but should be removed gently with mineral oil or shortening before resuming soaks or other measures.

### Powders

Powders like zinc oxide and talc are inert, and depend on their physical properties to reduce the friction of opposing skin surfaces and thereby soothe chafed sensitive skin areas. Others, like sulfur and salicylic acid, provide a specific medicinal effect. Powders, inert or active, should not be used in treating acute vesicular or weeping eruptions.

### Tinctures and Paints

Tinctures and paints should be used on circumscribed areas when water-insoluble medicaments are indicated but ointments are contraindicated, or in chronic, dry, fissured tinea pedis, or tinea cruris.

To these basic facts about ointments and other topical therapies should be added a few important general guidelines in treating skin disorders:

1. The mildest treatment is often the most effective; avoid overtreating.

2. The more inflamed and acute the dermatitis, the blander therapy should be.

3. Skin sensitizers such as topical penicillin, sulfonamides, and local anesthetic agents should not be used.

4. Add to the basic therapy of

ointment, compress, or whatever, only those ingredients that are specifically called for. "Shot-gun" preparations should be avoided; an ointment containing a steroid, antifungal, antibacterial, and anesthetic agent, as well as tar and sulfur, trusts more to luck than to a correct diagnosis.

## QUESTIONS AND ANSWERS

Q. *A patient of mine has a condition of the scalp characterized by copious unsightly branny scales and crusts, and intense intermittent itching that, with all his rubbing and scratching, has resulted in lichenification. He balks about using a crude coal tar ointment because it mats his hair and has an obnoxious odor. Except for his scalp condition, he's in good health. Could you suggest a topical that would help and also be acceptable to the patient?*

A. I agree with the patient, ointments are messy to use on the scalp. The water-miscible creams, one containing sulfur and salicylic acid for example, are usually more acceptable. Probably the easiest and best form to use is a water-miscible lotion. Depending upon the patient's skin the lotion can be an oily or non-oily one. One that I find particularly useful consists of crude coal tar solution (liquor carbonis detergens) 5%, salicylic acid 3%, castor oil (or olive oil) 5-10% and alcohol 70% – q.s. In addition, you can use a 1% hydrocortisone ointment in the scalp for the lichenification which has resulted in the patient you describe.

Q. *Why do you suggest using tinctures or paints instead of ointments as vehicles in treating chronic, dry fissured tinea pedis or cruris? Wouldn't the lubricating, softening property of an ointment be of benefit in these cases?*

A. Some ointments, such as the water-miscible ones, might be used once in a while overnight. Generally, however, ointment vehicles are occlusive and by impeding normal evaporation and loss of heat from the skin tend to promote favorable conditions for fungus growth.

Q. *When may dermatoses be bandaged?*

A. Dermatoses may be bandaged if soft muslin is used. Clean material from old bedsheets or shirts is preferred over gauze because gauze will stick and is also too rough. Orthopedic stockinette may be used to hold the sheeting or shirting in place on the extremities. Acute vesicular dermatoses, for which compresses or baths are used, are, however, best left uncovered; when covering them is necessary, it can be done with a non-adherent sterile dressing (like Telfa) as would be used in treating a burn.

# PEDIATRICS

**Lewis A. Barness, M.D.**
**University of Pennsylvania**

*Lewis A. Barness is Associate Professor of Pediatrics at the University of Pennsylvania School of Medicine, and Acting Chief of Service at the Hospital of the University of Pennsylvania. He serves as Chief of Pediatrics at Philadelphia General Hospital and as Associate Physician at the Children's Hospital of Philadelphia. For last month's issue of* CONSULTANT, *Dr. Barness wrote on the problem of hypernatremia in infants; in this issue, he turns his attention to the treatment of glomerulonephritis.*

## PRACTICAL MANAGEMENT OF ACUTE GLOMERULONEPHRITIS IN CHILDREN

Acute glomerulonephritis is fairly common in children, accounting for about 5% of all pediatric hospital admissions. It is a serious illness and deserves serious attention. Too often, however, the attention it gets is excessive and complicates the child's life with restrictions that have no proven value. Except in the acute phase, no particular therapeutic regimen seems to produce better results than any other. It seems wise, therefore, to choose a method which causes the child the least possible hardship — not one which, by prolonged confinement to bed and undue concern for diet, hinders recovery and involves too long an absence from school. Here is the method I find satisfactory; it features, whenever possible, a minimum of bed rest, a free diet, and normal physical activity.

Diagnosing acute glomerulonephritis is usually not difficult. Typically, the child will have been brought for treatment because of gross hematuria, headache, and edema—usually two or three weeks after a sore throat, skin infection, or other infection. (In rare cases, no history of infection can be elicited.) Urinalysis shows many red blood cells, a 2+ or 3+ protein, and occasional granular or hyaline casts. The blood urea nitrogen is usually elevated, varying from 20 mg% to 150 mg% (values over 100 mg% suggest a chronic process). The erythrocyte sedimentation rate is almost invariably elevated; the serum cholesterol, slightly elevated; and the serum

albumin, slightly low. Nasopharynx cultures frequently reveal B-hemolytic group A streptococci, perhaps residuum from the preceding infection (antigen-antibody reaction to this organism is thought to be the cause of acute glomerulonephritis).

### If Hypertension Is Present

The most important factor to consider when planning treatment is hypertension. If it is present, we restrict the patient to bed, give phenobarbital, 3 mg. per lb. of body weight, and offer fluids ad lib. If the blood pressure does not return to nearly normal limits within four hours, we place the patient on a low-sodium diet and give reserpine, 0.1 mg/kg, and apresoline, 0.15 mg/kg, intramuscularly. This usually lowers the blood pressure promptly. The blood pressure tends to gradually rise again, in which case the doses of reserpine and apresoline are repeated every 12 hours, or as often as every 8 hours if necessary.

Almost all patients respond to this regimen, but in rare instances there is no blood pressure response. If there is not, we use still another measure: magnesium sulfate, 0.1 gm/kg in a 50% solution, intramuscularly. This may be repeated every four hours for a total of not more than three doses. Incidentally, we have not found chlorothiazide helpful in hypertension from acute nephritis.

If the heart is enlarging or if the blood pressure drops suddenly without drug therapy, we begin rapid digitalization. If the patient is convulsing, we repeat the phenobarbital and may give 3 cc. of paraldehyde intramuscularly. On rare occasions, in the child with hypertensive encephalopathy due to acute nephritis, we have carefully performed a lumbar puncture, removing only one or two *drops* of spinal fluid; this measure dramatically stops the seizures and immediately lowers the blood pressure.

*Once the blood pressure has returned to normal* — or if the patient begins treatment with normal blood pressure — we adopt a more relaxed attitude. We give the child procaine penicillin, 300,000 units intramuscularly daily, because almost all children still harbor streptococci in the acute phase of the disease. We place the child on a free diet, without restriction of salt, protein, or fluid, because *we feel that it is more important that he eat, rather than be concerned with what he eats.* If he is oliguric, on the first day, we urge fluids up to 1000 cc. over his output, and if he is vomiting, we give these fluids intravenously. If oliguria persists, after the first day we restrict fluids to 300 cc. over the measured output.

### The Question of Bed Rest

The next point about treatment is a controversial one — when to allow the patient out of bed. We do not want too-early ambulation to impair healing of the diseased kidneys, but at the same time, how useful (and how practical) is prolonged bed rest? Our policy is a liberal one, perhaps because we have seen patients with glomerulonephritis who had been kept in bed needlessly long — with no beneficial effects, and some harmful ones. As soon as the patient's appetite returns and he says he's hungry, we obtain an erythrocyte sedi-

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1. Lemere, F.: Tranylcypromine ('Parnate'), A New Monoamine Oxidase Inhibitor, Am. J. Psychiat. *117*:249 (Sept.) 1960.
2. Petersen, M.C.: Depression: Treatment with a New Antidepressant—Tranylcypromine, report accompanying scientific exhibit at the 116th A.P.A. Meeting, Atlantic City, New Jersey, May 9-13, 1960.
3. Roebuck, B.E., and Maccubbin, H.P.: Treatment of Depression with Tranylcypromine, report accompanying scientific exhibit at the 13th Annual A.M.A. Clinical Meeting, Dallas, Texas, Dec. 1-4, 1959.


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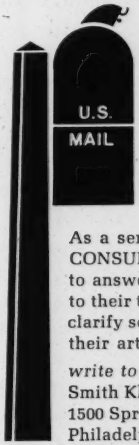
mentation rate and an Addis count. On the next day, we allow him out of bed. If his sedimentation rate does not increase over 10% of what it was on the previous day, or if his Addis count does not rise over 20%, we send him home on limited activity for one week. At the end of the week, we re-examine him for general well being, blood pressure, appetite, absence of vomiting, tiredness, and sedimentation rate. If his general health is satisfactory, and the sedimentation rate has not increased since discharge, he is then allowed to go back to school for half days. If, after a week, he is not tired in school, he is allowed back to full school activity, restricted only from strenuous activities such as gym, bicycle riding, and football.

During the recovery period, we compare physical examinations and urinalyses at monthly intervals. At the same time, we give injections of long-acting intramuscular penicillin through one complete respiratory-infection season, to safeguard against exacerbation. It is customary, and not a warning of exacerbation, for white cells to appear in the urine for a short time, as the hematuria disappears during the first or second month of disease. Proteinuria, hematuria, casts, and white cells generally disappear in a month or two, and the sedimentation rate may become normal in this time. However, full recovery may take longer, and we do not become concerned about progress as long as the laboratory findings return to normal within two years after onset of the disease.

With the above regimen, we have been able to release most of our patients from the hospital within 10 days or two weeks. Normally, they can return to full activity within a month or six weeks after onset of the disease. We have rarely seen a recurrence.

Prognosis for acute glomerulonephritis in children is almost always good. About 90-95% go on to complete remission without residua. Another 3-8% develop *chronic* glomerulonephritis, which may persist for 2 to 20 years or longer, with eventual death in renal failure. In the acute phase, 1-2% die, but usually as a result of hypertensive complications such as cardiac failure and hypertensive encephalopathy; only rarely does a child die of renal failure with the usual signs of uremia. The disease, of course, should not be treated casually. But on the other hand, treatment that is too restrictive—too concerned with diet and bed rest—does not decrease mortality, and only imposes needless hardships on the patient.

## CORRESPONDENCE

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# LARYNGOLOGY

**Raymond S. Rosedale, M.D.**
**Mercy Hospital, Canton, Ohio**

*Raymond S. Rosedale is a member of the Senior Staff, Otolaryngology, and Chief of the Department of Plastic Surgery of the Head and Neck, Mercy Hospital and Timken-Mercy Hospital, Canton, Ohio. He has served as Director of Education, Mercy Hospital, since 1938. He is a Diplomate of both the American Board of Pathology (1937) and the American Board of Otolaryngology (1940). Included among his professional affiliations are the American Academy of Ophthalmology and Otolaryngology, International College of Surgeons, American College of Chest Physicians, American College of Gastroenterology, and the American College of Allergists.*

## HOARSENESS— A SYMPTOM, NOT A DISEASE

Because hoarseness is a common symptom of mild disease, it is easily overlooked as a warning of potentially serious pathology of the larynx, systemic disease, or even intracranial disturbance. In chronic conditions especially, uncovering the cause of hoarseness correctly may actually prove life-saving to the patient.

Three simple steps need be taken: learn the causes of hoarseness; take a careful history; examine the structures of the larynx internally as well as externally.

Dr. Rudolf Nowara and I recently reclassified the causes of hoarseness on an anatomic-pathologic basis, the details of which are given in our original report.* The three main causes are listed here.

I. NEUROGENIC

A. Central

1. Thrombosis
2. Hemorrhage
3. Brain Trauma
4. Degeneration
5. Inflammation

B. Peripheral

1. Trauma
2. Tumors
3. Other Pressures

*Ohio State Medical Journal 56 (3):334-338, 1960.

II. INTRINSIC

1. Anomalies
2. Inflammations
3. Cysts
4. Degeneration
5. Trauma
6. Tumors
7. Edema

III. MISCELLANEOUS

Including myasthenia gravis, puberty, pregnancy, hysteria, vocal abuse, foreign bodies, local irritants.

**Hoarseness of Sudden Onset**

Hoarseness of sudden onset without pain is more often seen in middle aged and older people; its cause: a central small thrombosis. Quite frequently in such cases, hoarseness is first manifest on awakening, is of moderate degree, and tends to persist.

Hoarseness following laryngeal dyspnea is an indication of an acute allergic reaction which may be mild or grave. Impacted foreign bodies or noxious fumes and liquids may also produce hoarseness suddenly.

Prolonged or very forceful use of the larynx, as in cheering, screaming, etc., can cause subepithelial hemorrhage in a vocal cord and suddenly impair the quality of the voice.

Direct trauma may cause edema, fractures, or lacerations of the laryngeal components. Indirect trauma, such as the "whiplash" injury, may result in hoarseness, too. Sudden hoarseness follows damage to the recurrent laryngeal nerves in deep neck surgery.

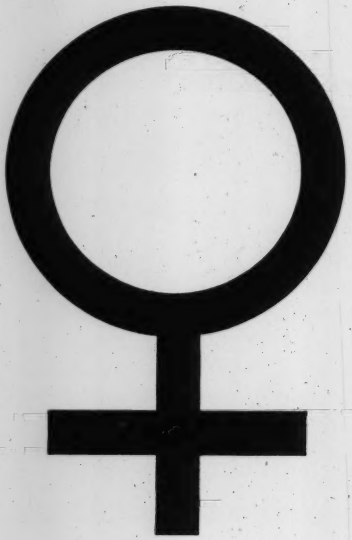
**Acute Hoarseness**

Acute hoarseness is commonly seen in acute inflammations of the respiratory tract, the other symptoms of which are well known. There are other causes; for example, acute ulcer of a vocal cord, in which severe pain, stabbing and knife-like in character, is also present. After a few days there may be expectoration of a blood-stained fibrin crust-pattern. Laryngeal ulcers require several weeks to several months for healing.

In the group of syndromes known as Avellis', Tapia, Hughling-Jackson, etc., due to intracranial thrombosis, or some other destructive lesion between the nucleus ambiguus and the jugular foramen, hoarseness may develop in a few hours or several days.

**Chronic Hoarseness**

Chronic hoarseness challenges the physician's diagnostic ability most. Hoarseness following an uncomplicated acute respiratory infection should not persist for more than three weeks. In this connection, an uncomplicated cold does not last more than two weeks and the average person does not have more than three or four colds a year. If "colds" last longer or recur more frequently, they are not "colds." Therefore hoarseness after a cold — persisting, becoming progressively worse, or recurring — must be investigated.



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From a report by Foster, H.M.: Am. J. Obst. & Gynec. 77:130 (Jan.) 1959.

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Note: In geriatric patients or in children always start with 5 mcg. daily and adjust dosage in increments no greater than 5 mcg.

| Indication | Recommended Starting Dose | Recommended Maintenance Dose |
|---|---|---|
| Hypometabolism Mild Hypothyroidism | 25 mcg. daily | 25-75 mcg. daily (Smaller doses may be fully effective in some patients.) |
| Myxedema | 5 mcg. daily | 50-100 mcg. daily |
| Female Reproductive Disorders | 25 mcg. daily | 25-50 mcg. daily |
| Male Infertility (Based on sperm count or sperm motility responses after two to four weeks of treatment at a given dosage level, the daily dosage may be increased by 5 or 10 mcg. If after further treatment the desired response has still not been obtained, the daily dosage may again be increased. Although total daily dosage usually need not exceed 25 mcg., as much as 50 mcg. daily may be used if necessary.) | 5 mcg. daily | 10-25 mcg. daily |
| Simple (non-toxic) Goiter | 5 mcg. daily | 25-75 mcg. daily |

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### Central Nervous System Disorders

Bulbar sclerosis, multiple sclerosis, cortical atrophy, arteriosclerosis, and syringomyelia may cause chronic hoarseness. General examination, local examination, and history should lead the physician to suspect one of these disorders.

### Hoarseness in Chronic Sinusitis and Allergy

Chronic sinusitis with postnasal discharge is suggested by the history of nasal obstruction, postnasal drip, and the finding of reddened so-called lateral bands on the posterior wall of the pharynx. Chronic respiratory tract allergy is a common cause of hoarseness. A characteristic history of shifting nasal obstruction, burning sensation and itching of the nose and eyes, mucoid or watery nasal or postnasal discharge signifies the probable presence of upper respiratory tract allergy. The finding of swollen gray violaceous nasal mucosa with mucous blobs, together with a family history of allergy, or past personal history of allergic conditions as asthma, hives, hay fever, eczema, recurrent diarrhea, and purposeless cough, indicates a probable diagnosis of chronic respiratory tract allergy.

### Chronic Hoarseness in Chest Disease

Repeated forceful coughing irritates the vocal cords mechanically. Frequent lavage of them with the purulent secretions of true bronchitis, bronchiectasis, lung abscess, tuberculosis and fungus infections may cause hoarseness.

Aortic aneurysm, dilatation of the left auricle, and pericardial effusion may cause hoarseness through pressure on the left recurrent laryngeal nerve.

### Miscellaneous Causes

Other causes of hoarseness may be quite unrelated in etiology. They include the hoarseness of puberty, pregnancy, chronic myositis, myasthenia gravis, myasthenia laryngis, scleroderma, senility, hyperkeratosis, and arthritis of the larynx. Misuse of the voice, overuse of tobacco, the industrial environment of irritating atmospheres, chronic overindulgence of alcoholic beverages, and mouth breathing may also be at fault.

### Benign Tumors of the Larynx

Chronic hoarseness in children in the absence of allergy or respiratory infection is most often due to papilloma of the larynx. Papillomata may be single but more often are multiple. After removal they tend to recur.

Singers may develop nodules, usually single but sometimes bilateral, on the vocal cords. They are painless but impair the singing voice.

Chronic granulomata, not infrequently the result of subepithelial hemorrhage, are sometimes mistaken for benign tumors. True benign tumors such as adenomata are rare. So are cysts. With cysts, as well as with papillomata, continued enlargement of the lesions may be accompanied by dyspnea and cyanosis.

### Malignant Tumors of the Larynx

Squamous cell carcinoma is the most likely invader to be found; malignant tumors of the epiglottis and supraglottic area are uncommon, and sarcoma

and adenocarcinoma are rare. Squamous cell carcinoma announces itself with inexorable, stealthy progressive hoarseness—without pain, dyspnea, or bleeding until late in the course of the disease. Squamous cell carcinoma of the larynx is one of the most curable cancers. In early stages it is confined to a vocal cord, and requires removal of part or all of the involved vocal cord; later in the disease, the cartilaginous box containing the vocal cords may have to be removed. Such measures ordinarily effect a cure. The author respects the usefulness of radiotherapy but space does not permit further consideration of its role.

An oft-repeated statement by Drs. Jackson and Jackson regarding intrinsic cancer of the larynx bears repeating: "In this stage cancer is curable in 82 per cent of the cases but unfortunately in all but 19 per cent it is overlooked. The only symptom is slight hoarseness, usually intermittent. Frequent or persistent hoarseness in an adult should be regarded as cancer until proven otherwise by proper diagnostic methods. Total laryngectomy would be a rare operation if all intrinsic laryngeal cancers were discovered in this stage." Early diagnosis with earlier treatment results in a high cure rate.

### Examination of the Larynx

The larynx can be examined by external palpation, X-ray, and inspection of the interior. Palpation is not helpful except in arthritis, advanced malignancies and trauma. Skillful X-ray interpretation is not especially helpful in early tumors or cysts but should be sought.

Indirect or mirror examination can be done with just a little practice by all physicians. A warmed #8 or #9 mirror is held above the pharyngeal airway while the tongue is held forward by the examiner or patient. The patient is instructed to "pant like a puppy on a hot day." A head mirror serves as a light source. The patient is then instructed to say "Eeee" in a high voice, so as to adduct the vocal cords. Sometimes it may be necessary to spray the pharyngolarynx with a topical anesthetic to prevent gagging. During the examination the contour, color and movement of all parts of the larynx should be observed. Finally, if the indirect examination is not completely satisfactory a direct examination of the larynx is mandatory.

### Findings

Tumors, ulcers and cysts will be obvious. In chronic laryngitis the structures of the larynx will be dry, granular, and sometimes red. Precancerous lesions, such as leukoplakia, may be observed. In allergies there will be diffuse pale swelling. In hypothyroidism there may be diffuse wetness. There may be various forms of vocal cord paresis or paralysis, unilateral or bilateral, and/or failure to adduct, abduct or tense. Tumors should be biopsied. Singer's nodes should be left for specialists.

In summary, when we see a patient with hoarseness, we should think of the causes of hoarseness; remember that it is a symptom and not a disease; consider thoroughly and examine carefully those in whom it persists for more than three or four weeks.

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**Rogers, H.L.: Postgrad. Med. *26*:85 (July) 1959.**

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Prescribing information adopted Jan. 1961.

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SPECIAL FEATURE

**Paul E. Chodoff, M.D.**
**George Washington University**

*Paul E. Chodoff is Assistant Clinical Professor of Psychiatry at George Washington University School of Medicine in Washington, D. C. He received his medical training at Jefferson Medical College, Philadelphia General Hospital, Montefiore Hospital, and St. Elizabeth's Hospital in Washington. He serves as consultant to the National Institutes of Health and the Veteran's Administration Hospital in Washington, and is attending physician at the George Washington University Hospital. During recent years, Dr. Chodoff has devoted special attention to the psychiatric problems of chronic and incurable illness.*

# UNDERSTANDING THE CHRONICALLY ILL PATIENT

Patients with chronic illness or persistent disability from diseases such as multiple sclerosis, coronary artery disease, or arthritis, or from crippling injury, pose an especially challenging treatment problem – as you know, if you have an average medical practice. Some need help but will not accept it. Others cannot be helped medically, but demand – and need – help. Briefly, let us delve into the psychiatric aspects of chronic illness and, in doing so, examine some factors which may help in dealing with such patients.

The chronically ill or disabled person, in our competitive culture, must contend with a great deal more than simply the physical consequences of his disability. His chief problem, in fact, may very well arise from altered relationships with others, rather than from decreased physical capacity. As a result of his illness, or the accident which befell him, the patient tends to become much more dependent on others around him. This increased dependency will be accompanied by a certain amount of resentment which he may be unable to cope with, express, or even be aware of. He can react to the threat to his previous personality organization posed by his increased dependency in various ways. But unless he is one of the fortunate few who have unusual emotional resources and inner stability, his reaction will probably tend in one of two directions.

First, the patient may make substantial use of the personality defense of *denial* – and will fight the conflicts engendered by his disability by trying to prove himself as good as the unhandicapped; by using slogans ("You're as good as any-

one") or believing in magic remedies; and sometimes by blaming himself or others for his disease, since by doing so he avoids admitting its impersonal nature and his powerlessness against it. This group of patients will often win praise from those around them for their efforts and may be brought to your attention because they are trying to do too much, and thus exhausting and harming themselves.

The other direction which disabled or chronically ill people may take to deal with their conflicts, is, instead of denying their handicap and their dependency, to *exaggerate their helplessness* and make only token efforts at self-help. Thus, they derive an advantage from their illness by being taken care of by those around them. Such patients seem to have "given up," make unaccountably slow progress in rehabilitating themselves, and sometimes show a morbid sense of defeat.

Probably no patient uses one or the other method exclusively. Any handicapped person may alternate between these methods, just as the healthiest of us sometimes find ourselves denying unpleasant aspects of reality or temporarily playing a helpless and regressive role. The problems of disabled or chronically ill people are often augmented, however, by the fact that people about them react to them in an unrealistic, sometimes even hostile, manner. This happens because handicapped people may set off emotional conflicts in the healthy person, as for instance, by activating conflicts about their own impulses to be dependent. Many healthy people have a stereotyped, although vague, picture of how they expect the disabled to act and feel. If the disabled person does not conform to the stereotype, his behavior may give rise to unfavorable reactions in some of those around him.

### The Physician's Attitude

It is important to realize, at this point, that physicians are not immune to this kind of reaction, despite a medical education. To discharge our therapeutic function as physicians, with some hope of being useful rather than merely busy, we need above all an emphatic understanding of the chronically ill, the altered world in which they live, their needs, and the methods they use to meet their problems.

Our first task is not an easy one or one that can be learned as easily as drugs and dosages. Before we can be truly helpful, we must be aware of the difference between the treatment of the acutely ill patient, who is struggling for life, and treatment of the *chronically* ill patient, who is struggling not for his life, but for self-respect in the world of men. We should try to put aside illusions of omnipotence, and remember that the patient will adjust to his illness in ways which vary according to his personality and inner resources—not in ways which we think he should. Some patients are braver and have more resources than others, and the kinds of long-term adjustments they make will certainly vary. Finally, I believe we should set aside the notion, so prevalent in our society, that dependence on others is always an evil to be avoided as assiduously as a demonic possession. *Some patients should be dependent*—just as others may be better off if encouraged to be self-reliant. *The best treatment we can offer some chronically ill patients is to accept*

*their dependence on others and on us.*

**Suggestions for Management**

Chronic illness is not only a challenging medical problem, it is also a growing one. There are 5.3 million chronically ill Americans today. Seventy-five years ago, only 1 out of every 15 persons who died had been chronically ill or disabled. Today, more than half have been. This means we are going to be faced more and more with managing chronically ill patients. To do so effectively, I would recommend these general principles of management:

1. By a leap of the imagination, try to put yourself in the world of your patient so that you may understand his needs as fully as possible—especially his dependent needs and the methods he employs to deal with them.

2. Become as aware as possible within the limits of your capacity for self-knowledge of the blind spots in your own personality (for instance the possible need for omnipotence) so that their interference in your relationship with your chronic patients can be minimized.

3. Inform yourself of the ancillary and paramedical agencies in your community (such as social work, vocational guidance, recreational, and welfare agencies) which can help your patients.

4. Be prepared to take an active role, if need be, in counseling and advising the family of your patient about their own attitudes and about any environmental changes that may seem necessary for the patient's welfare.

5. Remember the fundamental difference between remedial and chronically ill patients. To the former you bring treatment and hope of cure; to the latter, you bring ministering and hope only of amelioration. Remember, the latter goal is as honorable as the first.

# DEXAMYL® SPANSULE®

brand of sustained release capsules

## daylong control of appetite plus mood improvement

FORMULA: Each 'Dexamyl' *Spansule* capsule No. 1 contains Dexedrine® (brand of dextro amphetamine sulfate), 10 mg.; amobarbital (Warning, may be habit forming), 1 gr. Each 'Dexamyl' *Spansule* capsule No. 2 contains 'Dexedrine' (brand of dextro amphetamine sulfate), 15 mg.; amobarbital (Warning, may be habit forming), 1½ gr. The active ingredients of the 'Spansule' capsule are distributed among hundreds of minute pellets with varying disintegration times. A therapeutic dose is released immediately and the remaining medication, released slowly and without interruption, sustains the effect for 10 to 12 hours.

INDICATIONS: (1) For control of appetite in overweight; (2) for mood elevation in mild depressive states.

RECOMMENDED DOSAGE: One 'Dexamyl' *Spansule* capsule taken in the morning.

SIDE EFFECTS: Insomnia, excitability and increased motor activity are infrequent and ordinarily mild.

CAUTIONS: Use with caution in patients hypersensitive to sympathomimetic compounds or barbiturates and in coronary or cardiovascular disease, or severe hypertension.

Prescribing information adopted January 1961.

*Smith Kline & French* SK&F *Laboratories, Philadelphia*

# THORAZINE®
brand of chlorpromazine

# PRESCRIBING INFORMATION

## Tranquilizer • Antiemetic • Potentiator

The wide diversity of clinical applications in which 'Thorazine' is valuable, as either a specific or an adjuvant, is due to its three fundamental clinical properties: (1) its capacity to alleviate anxiety, tension and agitation without dulling mental acuity, (2) its ability to potentiate sedatives, narcotics and anesthetics, and (3) its profound antiemetic effect.

The tranquilizing effect of 'Thorazine' accounts for its usefulness in somatic conditions where emotional stress is a factor, as well as in mental and emotional disturbances *per se*.

## INDICATIONS

The value of 'Thorazine' is established in the following conditions:

**Moderate to severe mental and emotional disturbances of everyday practice**, particularly those disturbances marked by agitation, tension, apprehension, excitement, or anxiety.

**Somatic conditions complicated by emotional stress**, such as arthritis, tuberculosis, severe tension headaches, gastrointestinal disorders, dermatologic conditions, status asthmaticus and severe asthma.

**Hospitalized psychiatric patients**, to control agitation, dispel delusions and hallucinations, and at the same time to restore or increase the patient's capacity to respond to psychotherapy.

**Nausea, vomiting and hiccups**, with dramatic results in severe and refractory cases.

**Acute or chronic alcoholism**, to control agitation, delirium tremens, and nausea and vomiting.

**Cancer**, as an adjuvant, to control apprehension, suffering due to pain, and nausea and vomiting.

**Intractable pain**, to reduce suffering and to potentiate narcotics or sedatives.

**Obstetrics**, as an adjuvant, to control apprehension, pain, and nausea and vomiting. 'Thorazine' allows a reduction in the amounts of the drugs ordinarily used in obstetrical management, thus lessening the risk of respiratory depression in mother and infant.

**Surgery**, as an adjuvant, to control anxiety and apprehension, pain, and nausea and vomiting; and to reduce by potentiation the amounts of narcotics, sedatives and anesthetics needed.

## ADULT DOSAGE AND ADMINISTRATION

Dosage should always be adjusted to the response of the individual and the severity of the condition. It is important to increase dosage until symptoms are controlled or side effects become troublesome.

**Mental and Emotional Disturbances of Everyday Practice** – Depending on severity, *starting oral dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. After a day or two, dosage may be increased by increments of 20 mg. to 50 mg. daily, at semiweekly intervals (increase should be more gradual in emaciated or senile patients) until achieving maximum clinical response. Continue dosage at this level for at least two weeks; then it can usually be reduced to a maintenance level. A daily dosage of 200 mg. is "average," but in some cases, such as discharged mental patients, daily dosages as high as 800 mg. may be necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If necessary, and if no hypotension occurs, repeat the initial dose in one hour. Subsequent dosages should be oral, starting at 25 mg. to 50 mg. t.i.d.

**Somatic Conditions Complicated by Emotional Stress**–*Starting oral dosage* is 10 mg. to 25 mg. t.i.d. or q.i.d. Increase gradually by 10 mg. to 25 mg. increments at semiweekly or weekly intervals. *Starting intramuscular dosage* is 25 mg. (1 cc.), repeated after one hour if necessary and if no hypotension occurs.

**Hospitalized Psychiatric Patients** – ***Acutely agitated, manic, or disturbed patients:*** *Starting intramuscular dose* is 25 mg. (1 cc.). If no marked hypotension occurs, an additional 25 mg. to 50 mg. injection may be given after one hour. Subsequent intramuscular dosages may be increased gradually over a period of several days – even up to 400 mg. q4-6h in exceptionally severe cases – until the patient is controlled. (In elderly or emaciated patients the dosage should be increased more slowly than in other patients.) Usually the patient becomes quiet and cooperative within 24 to 48 hours after the initial dose, at which time oral doses may gradually be substituted for intramuscular doses (mg. for mg. or higher). Even if control is not complete, oral doses may gradually replace intramuscular doses. During this period, oral dosage should be increased rapidly until the patient is calm. Usually an *oral dose* of 500 mg. a day is sufficient but, if necessary, the dosage may be gradually increased still further to 2,000 mg. a day or higher. ***Less acutely agitated patients:*** *Starting oral dose* is 25 mg. t.i.d. Subsequently, increase the amount gradually until an effective dosage is reached – usually 400 mg. daily is sufficient. ***Duration of therapy:*** It is important to determine the optimal dosage regimen and to continue treatment long enough for maximum clinical response. Maximum improvement is sometimes not apparent until after weeks or even months of therapy.

**Nausea and Vomiting** – *Starting oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n., and may be increased if necessary. *Starting intramuscular dose* is 25 mg. (1 cc.). If no hypotension occurs subsequent doses of 25 mg. to 50 mg. q3-4h, p.r.n., may be given until vomiting is checked. Then replace intramuscular administration with oral. *Starting rectal dosage* is one 100 mg. suppository q6-8h, p.r.n. In some patients, one-half this dose may be sufficient.

**Hiccups** – *Starting oral dosage* is 25 mg. to 50 mg. t.i.d. or q.i.d. If after 2-3 days symptoms persist, *an intramuscular dosage* of 25 mg. to 50 mg. (1-2 cc.) may be used. *Use intravenous administration* only when symptoms still persist. By slow infusion, 25 mg. to 50 mg. (1-2 cc.) should be administered in 500 cc. to 1,000 cc. of physiologic saline solution, with the patient kept flat in bed. Follow blood pressure closely.

**Alcoholism** – ***Severely agitated patients:*** *Starting intramuscular dose* is 25 mg. to 50 mg. (1-2 cc.). Repeat initial dose if necessary and if no hypotension occurs. Start subsequent oral dosages at 25 mg. to 50 mg. t.i.d. ***Agitated but manageable patients:*** *Starting oral dose* is 50 mg., followed by 25 mg. to 50 mg. t.i.d. ***Ambulatory patients with withdrawal symptoms or sober chronic alcoholics:*** *Starting oral dose* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Patients in a stuporous condition should be allowed to sleep off some of the effects of the alcohol before 'Thorazine' is administered.

**Cancer and Pain** – ***Severe pain:*** *starting intramuscular dosage* is 25 mg. (1 cc.) b.i.d. or t.i.d. ***Milder pain:*** starting oral *dosage* is 10 mg. t.i.d. or q.i.d., or 25 mg. b.i.d. or t.i.d. Because 'Thorazine' potentiates their action, reduce the dosage of narcotics or sedatives to ¼ to ½ of the pre-'Thorazine' level.

**Obstetrics** – *Intramuscular dose* in labor and delivery is 12.5 mg. to 25 mg. (0.5-1 cc.), administered when dilation of the cervix reaches 3 to 5 centimeters or when strong labor is established. At the same time (but not mixed in the syringe with 'Thorazine'), ¼ to ½ the usual dose of a narcotic or sedative and, if desired, 0.4 mg. of scopolamine may be administered. Depending upon blood pressure, respiration and the general condition of the patient, the initial 'Thorazine' dose (alone or with reduced amounts of the other agents) may be repeated in 3 to 5 hours if necessary.

**Surgery** (Adults) – ***Preoperatively,*** *oral dose* is 25 mg. to 50 mg., 2 to 3 hours before the operation. *Intramuscular dose* is 12.5 mg. to 25 mg. (0.5-1 cc.), 1 to 2 hours before the operation. ***During surgery*** 'Thorazine' should be administered only if needed to control nausea and vomiting, retching, hiccups, or other acute symptoms. *Intramuscular dose* is 12.5 mg. (0.5 cc.), repeated in ½ hour if necessary and if no hypotension occurs.

*Intravenous dose* should be no more than 2 mg. per fractional injection, with injections at not less than 2-minute intervals. Also, it should not exceed 25 mg. 'Thorazine' should be diluted to 1 mg./cc. (1 cc. mixed with 24 cc. of physiologic saline solution). ***Postoperatively,*** *oral dosage* is 10 mg. to 25 mg. q4-6h, p.r.n. *Intramuscular dosage* is 12.5 mg. to 25 mg. (0.5-1 cc.), repeated in one hour if necessary and if no hypotension occurs.

## PEDIATRIC DOSAGE AND ADMINISTRATION

**Nausea and Vomiting, Behavior Disorders and Pain** – *Oral dosage* is on the basis of ¼ mg./lb. of body weight q4-6h, until symptoms are controlled (i.e., for 40 lb. child–10 mg. q4-6h). Calculate 'Thorazine' Syrup dosage at 10 mg./5 cc. tsp. *Rectal dosage* is on the basis of ½ mg./lb. of body weight q6-8h, p.r.n. (i.e., for 20-30 lb. child–half of a 25 mg. suppository q6-8h). *Intramuscular dosage* is on the basis of ¼ mg./lb. of body weight q6-8h, p.r.n. In children up to 5 years (or 50 lbs.)–not over 40 mg./day. In children 5-12 years (or 50-100 lbs.)–not over 75 mg./day.

**Pain**–Because 'Thorazine' potentiates the action of narcotics and sedatives, reduce the dosage of these agents to ¼ to ½ of the pre-'Thorazine' level.

**Behavior Disorders**–In severe cases, 50-100 mg. daily has been used and, in older children, 200 mg. or more daily may be required.

**Surgery (Children)** – ***Preoperatively,*** dose is on the basis of ¼ mg./lb. of body weight given either orally 2 to 3 hours before the operation, or intramuscularly 1 to 2 hours before. ***During surgery,*** the dose is on the basis of ⅛ mg./lb. of body weight, repeated in ½ hour if necessary and if no hypotension occurs. The intravenous dose should be no more than 1 mg. per fractional injection, with injections at not less than 2-minute intervals. Intravenous dosage during surgery should not exceed recommended intramuscular dosage and should always be diluted to 1 mg./cc. ***Postoperatively,*** dosage is on the basis of ¼ mg./lb. of body weight, either orally q4-6h, p.r.n., or intramuscularly, a single dose repeated in one hour if necessary and if no hypotension occurs.

## NOTES ON PARENTERAL ADMINISTRATION

Except for acute ambulatory cases, parenteral administration should generally be reserved for bedfast patients. Parenteral administration should always be made with the patient lying down and remaining so for at least ½ hour afterward because of possible hypotensive effects. The injection should be given *slowly, deep* into the upper outer quadrant of the buttock. If irritation and pain at the site of injection are problems, dilution of 'Thorazine' Injection with physiologic saline solution or 2% procaine solution may be helpful. Subcutaneous administration is not advisable, and care should be taken to avoid injecting undiluted 'Thorazine' Injection into a vein. Intravenous administration is recommended only for severe hiccups and surgery.

Because contact dermatitis has been reported, avoid getting the solution on hands or clothing.

## SIDE EFFECTS

The drowsiness caused by 'Thorazine' may be unwanted in some patients. It is usually mild to moderate and disappears after the first or second week of therapy. If, however, drowsiness is troublesome, it can usually be controlled by lowering the dosage or by administering small amounts of dextro amphetamine.

Other side effects that have been reported occasionally are dryness of the mouth, nasal congestion, some constipation, miosis in a few patients and, very rarely, mydriasis. Mild fever (99°F.) may occur occasionally during the first days of therapy with large intramuscular doses. During 'Thorazine' therapy some patients have an increased appetite and gain weight. Usually these patients reach a plateau beyond which they do not gain further weight.

## CAUTIONS

**Jaundice:** In the more than 14 million patients who have been treated with 'Thorazine' in the United States, the incidence of jaundice–regardless of indication, dosage, or mode of administration–has been low. Few cases have occurred in less than one week or after six weeks. Jaundice due to 'Thorazine' is of the so-called "obstructive" type; is without parenchymal damage; and is usually promptly reversible upon the withdrawal of 'Thorazine'. Because detailed liver function tests of 'Thorazine'-induced jaundice give a picture which mimics extrahepatic obstruction, exploratory laparotomy should be withheld until sufficient studies confirm extrahepatic obstruction.

**Agranulocytosis:** Agranulocytosis, although rare, has been reported in patients on 'Thorazine' therapy. Patients receiving 'Thorazine' should be observed regularly and asked to report at once the sudden appearance of sore throat or other signs of infection. If white blood counts and differential smears give an indication of cellular depression, the drug should be discontinued, and antibiotic and other suitable therapy should be instituted. Because most reported cases have occurred between the fourth and the tenth weeks of treatment, patients on prolonged therapy should be observed particularly during that period.

A moderate suppression of total white blood cells is sometimes observed in patients on 'Thorazine' therapy. If not accompanied by other symptoms, it is not an indication for discontinuing 'Thorazine'.

**Potentiation:** 'Thorazine' prolongs and intensifies the action of many central nervous system depressants, such as barbiturates and narcotics. Consequently, it is advisable to stop administration of such depressants before initiating 'Thorazine' therapy. Later the depressant agents may be reinstated, starting with low doses, and increasing according to response. Approximately ¼ to ½ the usual dosage of such agents is required when they are given in combination with 'Thorazine'. (However, 'Thorazine' does not potentiate the anticonvulsant action of barbiturates. In patients who are receiving anticonvulsants, the dosage of these agents–including barbiturates–should not be reduced if 'Thorazine' is started. Rather, 'Thorazine' should be started at a very low dosage and increased, if necessary.)

**Hypotensive Effect:** Postural hypotension and simple tachycardia may be noted in some patients. In these patients, momentary fainting and some dizziness are characteristic and usually occur shortly after the first parenteral dose, occasionally after a subsequent parenteral dose–very rarely after the first oral dose. In most cases, prompt recovery is spontaneous and all symptoms disappear within ½ to 2 hours with no subsequent ill effects. Occasionally, however, this hypotensive effect may be more severe and prolonged, producing a shock-like condition. In consideration of possible hypotensive effects, the patient should be kept under observation (preferably lying down) for some time after the initial parenteral dose. If, on rare occasions, hypotension does occur, it can ordinarily be controlled by placing the patient in a recumbent position with head lowered and legs raised. If it is desirable to administer a vasoconstrictor, 'Levophed' and 'Neo-Synephrine'★ are the most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may reverse the usual elevating action of these agents and cause a further lowering of blood pressure.

**Antiemetic Effect:** The physician should always bear in mind that the antiemetic effect of 'Thorazine' may mask signs of overdosage of toxic drugs and may obscure diagnosis of conditions such as intestinal obstruction and brain tumor.

**Dermatological Reactions:** Dermatological reactions have been reported. Most have been of a mild urticarial type, suggesting allergic origin. Some of them appear to be due to photosensitivity, and it is advisable that patients on 'Thorazine' avoid undue exposure to the summer sun.

**Neuromuscular Reactions:** With very large doses of 'Thorazine', as frequently used in psychiatric cases over long periods, there have been a few patients who have exhibited neuromuscu-

★'Levophed' and 'Neo-Synephrine' are the trademarks (Reg. U.S. Pat. Off.) of Winthrop Laboratories for its brands of levarterenol and phenylephrine respectively.

lar reactions (extrapyramidal symptoms) which closely resemble parkinsonism. Such symptoms are reversible and usually disappear within a short time after the dosage has been decreased or the drug withdrawn. These neuromuscular reactions can also be controlled by the concomitant administration of standard anti-parkinsonism agents.

**Lactation:** Moderate engorgement of the breast with lactation has been observed in female patients receiving very large doses of 'Thorazine'. This, however, is a transitory condition which disappears on reduction of dosage or withdrawal of the drug.

## CONTRAINDICATIONS

In comatose states due to central nervous system depressants (alcohol, barbiturates, narcotics, etc.), and also in patients under the influence of large amounts of barbiturates or narcotics.

## AVAILABLE

**Tablets,** 10 mg., 25 mg., 50 mg. and 100 mg., in bottles of 50, 500 and 5000; 200 mg., for use in mental hospitals, in bottles of 500 and 5000. (Each tablet contains chlorpromazine hydrochloride, 10 mg., 25 mg., 50 mg., 100 mg., or 200 mg.)

**Ampuls,** 1 cc. and 2 cc. (25 mg./cc.), in boxes of 6, 100 and 500. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 6 mg.)

**Multiple-dose Vials,** 10 cc. (25 mg./cc.), in boxes of 1, 20 and 100. (Each cc. contains, in aqueous solution, chlorpromazine hydrochloride, 25 mg.; ascorbic acid, 2 mg.; sodium bisulfite, 1 mg.; sodium sulfite, 1 mg.; sodium chloride, 1 mg. Contains benzyl alcohol, 2%, as preservative).

**Spansule® capsules,** 30 mg., 75 mg., 150 mg. and 200 mg., in bottles of 30, 250 and 1500; also 300 mg., in bottles of 30 and 1500. (Each 'Spansule' capsule contains chlorpromazine hydrochloride, 30 mg., 75 mg., 150 mg., 200 mg., or 300 mg.)

**Syrup,** 10 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. (Each 5 cc. contains chlorpromazine hydrochloride, 10 mg.)

**Suppositories,** 25 mg. and 100 mg., in boxes of 6. (Each suppository contains chlorpromazine, 25 mg. or 100 mg.; glycerin, glyceryl monopalmitate, glyceryl monostereate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids, lecithin.)

**Concentrate** (for hospital use), 30 mg./cc., in 4 fl. oz. bottles, packages of 12 and 36; and in 1 gal. bottles. (Each cc. contains chlorpromazine hydrochloride, 30 mg.)

Prescribing information adopted January, 1961

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# COMPAZINE®

brand of prochlorperazine

# PRESCRIBING INFORMATION

## Antiemetic • Tranquilizer

'Compazine' provides a beneficial calming effect and prompt antiemetic action with unusual freedom from drowsiness and depressing effect. Clinical experience in several million patients has shown 'Compazine' to be promptly effective in low dosage, with minimal side effects in the dosage range recommended for everyday practice.

## INDICATIONS

*1. **Anxiety, tension, agitation,*** confusion, chronic alcoholism and behavior disorders in children.

*2. **Emotional stress associated with somatic conditions*** such as g.i. disorders, cardiovascular conditions, hypertension, menopause, premenstrual tension, neurodermatitis, arthritis, asthma, cancer, tuberculosis and tension headache.

*3. **Nausea and vomiting of widely varying causes*** such as pregnancy, postoperative conditions, viral gastroenteritis and other infectious conditions, irradiation therapy and motion sickness. In most patients, relief is provided within a short time after one oral dose.

*4. **In surgery and obstetrics*** to prevent or control: (a) nausea, vomiting and retching; and (b) fear, tension and restlessness.

*5. **In psychiatry*** to control agitation, anxiety, tension and confusion that may be seen in psychotic states.

## ADMINISTRATION AND USUAL DOSAGE

Dosage should be determined according to the severity of the condition and the response of the patient. It is important to begin therapy with the lowest recommended dosage. In hospitalized patients or those under adequate supervision, higher doses may be indicated.

## USUAL ADULT DOSAGE

**Tablets:** The usual starting dosage is 5 mg. three or four times daily. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. Dosage over 40 mg. daily should be used only in resistant cases.

**Spansule® sustained release capsules:** The usual starting dosage is one 15 mg. 'Spansule' capsule taken upon arising, or one 10 mg. 'Spansule' capsule in the morning and evening. Some patients may subsequently require dosage increased to one 30 mg. capsule in the morning. Dosage over 40 mg. daily should be used only in resistant cases. (B.i.d. dosage of the 30 mg. capsule should be limited to severe cases.)

Dosage recommendations for other oral forms of 'Compazine' may be applied to 'Compazine' *Spansule* capsules on the basis of the total daily dose in milligrams. (For example: one 15 mg. 'Compazine' *Spansule* capsule replaces 5 mg. 'Compazine' Tablets, t.i.d.) All strengths have the same *duration* of action. They differ only in *intensity* of therapeutic effect.

***In "morning sickness" of pregnancy,*** one 'Compazine' *Spansule* capsule taken before retiring affords antiemetic activity throughout the night and into the morning, thus protecting against "morning sickness."

The 15 mg. 'Compazine' *Spansule* capsule is ideal for once-a-day administration. The 10 mg. 'Compazine' *Spansule* capsule is ideal for twice-a-day (q12h) administration.

**Syrup:** 5 mg. to 10 mg. (1 to 2 teaspoonfuls) three or four times daily.

**Suppositories:** Usual dosage in adults is one 25 mg. 'Compazine' Suppository twice daily.

**Injection:** Total parenteral dosage in 24 hours should not exceed 40 mg.

***For intramuscular administration,*** an initial dose of 5 mg. to 10 mg. (1 to 2 cc.) of 'Compazine' Injection should be injected *deeply* into the upper outer quadrant of the buttock. Repeat, if necessary, at intervals of 3 to 4 hours. Pain at the site of injection has not been a problem. ***For intravenous administration,*** see surgery section. Dilution is not required. ***Subcutaneous administration*** is not advisable because of local irritation.

It is recommended that 'Compazine' Injection not be mixed with other agents in the syringe.

Dermatitis due to contact with 'Compazine' has not been a problem. However, it is recommended that nurses or others giving frequent injections take precautions to avoid getting the solution on their hands or clothing.

'Compazine' Injection should be protected from light, since exposure may cause discoloration. Slight yellowish discoloration will not significantly alter the potency or therapeutic efficacy. However, if markedly discolored, the solution should be discarded.

## IN SURGERY (Adults)

| ROUTE | DOSAGE |
|---|---|
| *preoperatively* | |
| Intramuscular injection | 5 mg. to 10 mg. (1-2 cc.) |

1 to 2 hours before induction of anesthesia. Repeat once in 30 minutes if necessary.

| ROUTE | DOSAGE |
|---|---|
| Intravenous injection | 5 mg. to 10 mg. (1-2 cc.) |

15 to 30 minutes before induction of anesthesia.

| | |
|---|---|
| Intravenous infusion | 20 mg. (4 cc.) per liter of isotonic solution |

Add to I.V. infusion 15 to 30 minutes before induction. Repeat once if necessary.

***during surgery***

| | |
|---|---|
| Intramuscular or Intravenous injection | 5 mg. to 10 mg. (1-2 cc.) |

When needed to control acute symptoms. Repeat once if necessary.

***postoperatively***

*To prevent* anxiety, nausea, vomiting, or emergence excitement, add to I.V. infusion: 20 mg. (4 cc.) per liter of isotonic solution.

*For immediate control* of acute nausea, vomiting, retching, or emergence excitement, inject 5 mg. to 10 mg. (1-2 cc.), I.V. or I.M. Repeat once if necessary.

## IN OBSTETRICS

'Compazine' dosage should be adjusted to the individual patient and her condition in accordance with the general use of the drug (i.e., 5 mg. to 10 mg. per dose; 15 mg. to 40 mg. per day). The following dosage suggestions should prove satisfactory for the majority of obstetric patients.

***To relieve anxiety or prevent vomiting during the first stage of labor,*** the usual dosage is 10 mg. of 'Compazine' by intramuscular injection. As labor progresses, or if it is prolonged, subsequent 10 mg. doses may be administered as needed. The total daily dose need rarely exceed 30 mg.

***To control postpartum anxiety or nausea and vomiting,*** the usual total daily dose of 'Compazine' is 15 mg. to 30 mg. administered orally or intramuscularly.

NOTE: 'Compazine' has no clinically significant potentiating effect on narcotics, anesthetics, or sedatives. However, because the 'Compazine' patient is calm and relaxed, it is sometimes possible to produce satisfactory analgesia with less than the customary amounts of these agents. This lack of potentiating effect also minimizes the risk of intensifying or prolonging the effect of residual anesthetics and other depressant agents used in surgery or labor and delivery.

As with intravenous administration of any surgical or obstetric adjuvant, the increased possibility of hypotension should be kept in mind if 'Compazine' is administered by either intravenous injection or infusion.

## USUAL CHILDREN'S DOSAGE

It is important always to use the lowest effective dosage, because as dosage is raised the possibility of side effects increases. There have been occasional cases of neuromuscular reactions (extrapyramidal symptoms) in children. These have been transitory and reversible.

**Nausea and vomiting** are usually controlled during the first day of therapy. Therefore more than one day's therapy is seldom necessary.

| Weight | Dosage | Not to exceed |
|---|---|---|
| Under 20 lbs. | not recommended | |
| 20-29 lbs. | 2.5 mg. once or twice a day | 7.5 mg. per day |
| 30-39 lbs. | 2.5 mg. b.i.d. or t.i.d. | 10.0 mg. per day |
| 40-85 lbs. | 2.5 mg. t.i.d. or 5 mg. b.i.d. | 15.0 mg. per day |

**For behavior disorders,** dosage may be increased gradually, if necessary, within the following daily limits:

2 to 6 years of age: Total daily dose should not exceed 20 mg.
6 to 12 years of age: Total daily dose should not exceed 25 mg.

**For rapid control of nausea and vomiting or behavior disorders:**

*Injection:* For children under 12 years of age, each dose should be calculated on the basis of 0.06 mg. of 'Compazine' per pound of body weight and should be administered by deep intramuscular injection. For example, a 40-pound child would receive an injection of 2.5 mg. (0.5 cc.). Control is usually obtained with a single dose.

## 'COMPAZINE' IN PSYCHIATRY

'Compazine' is indicated for control of agitation, anxiety, tension and confusion that may be seen in such conditions as schizophrenias; manic-depressive states, manic phase; severe personality disorders; involutional psychoses; degenerative conditions; and senile psychoses.

### ADULTS

**Oral psychiatric dosage:** *In relatively mild conditions,* as may be seen in private psychiatric practice or on outpatient clinics, the suggested starting dosage is 5 mg. t.i.d. or q.i.d. Some patients will respond better when subsequent dosage is raised to 10 mg. t.i.d. or q.i.d. *In moderate or severe conditions,* when patients are either hospitalized or under adequate supervision, the suggested starting dosage is 10 mg. t.i.d. or q.i.d. Dosage should be increased gradually until symptoms are controlled or side effects become bothersome. Experience has shown that when dosage is increased gradually (by small increments every two or three days) side effects either do not occur or are easily controlled.

Some patients will obtain satisfactory results on 50 mg. to 75 mg. of 'Compazine' daily. In more severe disturbances, the optimum dosage in most patients is 100 mg. to 150 mg. daily. With oral administration, response ordinarily becomes evident within a day or two. Longer periods of treatment are usually required before maximal improvement is obtained.

**I.M. psychiatric dosage:** For immediate control of severely disturbed adult patients, an initial dose of 10 mg. to 20 mg. (2-4 cc.) should be injected deeply into the upper outer quadrant of the buttock. If necessary, this dose should be repeated every 2 to 4 hours to gain control of the patient. Patients often respond shortly after the first injection. In resistant cases, the initial dose may be repeated hourly. More than three or four doses are seldom necessary. If, in rare cases, parenteral medication is indicated over a prolonged period, 10 mg. to 20 mg. (2-4 cc.) at 4- to 6-hour intervals is the usual dosage. Pain and irritation at the site of injection have rarely been encountered and some patients have been given the drug intramuscularly for periods of several weeks. After control is achieved by intramuscular administration, most patients can be switched to an oral form of the drug at the same dosage level or higher.

### CHILDREN *(2 to 12 years)*

**Oral psychiatric dosage:** The suggested children's starting dosage in psychiatry is 2.5 mg. (½ teaspoonful of syrup) two or three times daily, or 5 mg. (one teaspoonful of syrup or one 5 mg. tablet) twice daily, according to body weight. During the first day, the total daily dose should not exceed 10 mg. Dosage is then increased according to the patient's response. (2.5 mg. and 5 mg. suppositories are also available.)

*For ages 2 to 6,* the total daily dosage usually does not exceed 20 mg. *For ages 6 to 12,* the total daily dosage usually does not exceed 25 mg. Because extrapyramidal symptoms have been reported in children as well as in adults, it is important to use the lowest effective dosage.

## SIDE EFFECTS

In the dosage range recommended for everyday practice, side effects have been infrequent, transitory and usually mild. A few patients may experience a mild drowsiness when first taking 'Compazine'. There may also be occasional cases of dizziness,

skin reaction and neuromuscular reactions (extrapyramidal symptoms); rarely, hypotension.

*Neuromuscular Reactions*

Occasionally, neuromuscular reactions (extrapyramidal symptoms) have been observed with 'Compazine' therapy. It is important, therefore, to use the lowest effective dosage, because as dosage is raised the possibility of these reactions increases.

*Motor Restlessness:* A few patients on 'Compazine'—particularly those in whom dosage has been raised to higher levels—may experience a transient unpleasant stimulation or jitteriness, characterized by restlessness and insomnia. The dosage of 'Compazine' should not be increased while these side effects are present. Patients should be reassured that such effects are temporary and will disappear spontaneously. In those cases where the symptoms are particularly bothersome, reduction of dosage or the concomitant administration of a sedative may be helpful.

*Dystonias:* These neuromuscular reactions are seen in a significant percentage of hospitalized mental patients on high dosages. The muscles of the face and shoulder girdle may be selectively involved. Symptoms observed have included spasm of the neck muscles, extensor rigidity of back muscles, carpopedal spasm, eyes rolled back, trismus and swallowing difficulty. Despite some similarity to symptoms of serious neurologic disorders, these reactions are usually promptly reversible by temporary discontinuance of 'Compazine' therapy and administration of a sedative such as phenobarbital. The dosage and route of administration should be determined according to the severity of the symptoms. Patients should be reassured that the symptoms are transitory. Depending on the severity of the dystonia, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed. Note: It has been reported that injectable administration of Benadryl* may also be helpful.

*Pseudo-parkinsonism:* These neuromuscular reactions may resemble the classic parkinsonism syndrome. Treatment should include temporary discontinuance of 'Compazine' therapy and the administration of any standard anti-parkinsonism agent (see *PDR*). Patients should also be reassured that these symptoms are transitory. Depending on the severity of symptoms, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed.

## CAUTIONS

Clinical experience has demonstrated that 'Compazine', a phenothiazine derivative, has a wide margin of safety and that there is little likelihood of blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

The antiemetic action of 'Compazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

'Compazine' has no clinically significant potentiating action. However, if depressant agents are used in conjunction with this drug, the possibility of an additive effect should be kept in mind.

## CONTRAINDICATIONS

'Compazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

## AVAILABLE

There is a dosage form of 'Compazine' for every medical need.

**Tablets,** 5 mg. and 10 mg. and, for use in psychiatry, 25 mg., in bottles of 50, 500 and 5000. Each tablet contains 5 mg., 10 mg., or 25 mg. of prochlorperazine as the dimaleate.

**'Spansule' capsules,** 10 mg., 15 mg. and 30 mg., in bottles of 30, 250 and 1500; and, for use in psychiatry, 75 mg., in bottles of 30 and 1500. Each capsule contains 10 mg., 15 mg., 30 mg., or 75 mg. of prochlorperazine as the dimaleate.

**Ampuls,** 2 cc. (5 mg./cc.), in boxes of 6, 100 and 500. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 1 mg. sodium sulfite, 1 mg. sodium bisulfite, 8 mg. sodium phosphate and 12 mg. sodium biphosphate.

**Multiple-dose Vials,** 10 cc. (5 mg./cc.), in boxes of 1, 20 and 100. Each cc. contains, in aqueous solution: 5 mg. prochlorperazine as the ethanedisulfonate, 5 mg. sodium biphosphate, 12 mg. sodium tartrate, 0.9 mg. of sodium saccharin and 0.75% benzyl alcohol as preservative.

**Suppositories,** 2½ mg. (for young children), 5 mg. (for older children) and 25 mg. (for adults), in boxes of 6. Each suppository contains: 2½ mg., 5 mg., or 25 mg. of prochlorperazine with glycerin, glyceryl monopalmitate, glyceryl monostearate, hydrogenated cocoanut oil fatty acids, hydrogenated palm kernel oil fatty acids and lecithin.

**Syrup,** 5 mg./teaspoonful (5 cc.), in 4 fl. oz. bottles. Each 5 cc. contains 5 mg. of prochlorperazine as the ethanedisulfonate.

**Concentrate** (for hospital use), 10 mg./cc. in 4 fl. oz. bottles, cartons of 12 and 36. Each cc. contains 10 mg. of prochlorperazine as the ethanedisulfonate.

Prescribing information also available in *Compazine® Reference Manual, Physicians' Desk Reference,* or from your SK&F representative or your pharmacist.

Prescribing information adopted January 1961.

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# STELAZINE®

brand of trifluoperazine

# PRESCRIBING INFORMATION

## INDICATIONS

**In general practice and in psychiatry** 'Stelazine' is outstanding among tranquilizers because it relieves anxiety, agitation and tension—without sedation. Nor does it cause euphoria. 'Stelazine' is also effective in relieving anxiety either accompanying or causing somatic conditions. Where anorexia and insomnia are problems, 'Stelazine' usually produces a marked improvement in appetite and sleep patterns.

'Stelazine' provides a fast therapeutic response. On a convenient b.i.d. dosage regimen, many patients who have failed to respond to other agents, or have responded only poorly, are promptly relieved of their symptoms. With symptoms allayed, rapport with the physician is facilitated, and patients are more receptive to counselling or psychotherapy.

**In hospitalized psychiatric patients** 'Stelazine' produces rapid response in many diagnostic categories. These include acute and chronic schizophrenias, manic-depressive psychoses, involutional psychoses, chronic brain syndrome and mental deficiency.

'Stelazine' can combat psychotic symptoms without causing drowsiness. It can quiet hyperactive patients and activate withdrawn patients, and it has a marked beneficial effect on delusions and hallucinations.

'Stelazine' can rapidly terminate acute psychotic episodes. On the admissions service, intensive 'Stelazine' therapy often results in early discharges.

Also noteworthy is the effectiveness of 'Stelazine' in the treatment of hard-core, chronic and refractory schizophrenics. When administered to a group of such patients, it characteristically produces significant improvement in at least 30% to 40% of them.

## ADMINISTRATION AND DOSAGE

Dosage of 'Stelazine' should be adjusted to the needs of the individual.

*Trademark Reg. U.S. Pat. Off.: 'Benadryl' for diphenhydramine hydrochloride, Parke-Davis.

1. Adult Dosage for Use in Everyday Practice
Usual starting dosage is 1 mg. twice daily. Optimal dosage is 1 mg. or 2 mg. twice daily. In everyday practice it is seldom necessary to exceed 4 mg. daily.

Because of the inherent long action of 'Stelazine', patients may be controlled on convenient b.i.d. administration; some patients may be maintained on once-a-day administration.

2. Adult Dosage for Use in Psychiatric Practice
*oral (for office patients and outpatients with anxiety):* The usual starting dosage is 1 mg. b.i.d. In some cases, a better response is achieved on 2 mg. b.i.d. In the treatment of these patients, it is seldom necessary to exceed 4 mg. a day. (Some patients with more severe disturbances, and discharged mental patients, may require higher dosages.) In some patients, maintenance dosage can be reduced to once-a-day administration.

*oral (for patients who are either hospitalized or under adequate supervision):* The usual starting dosage is 2 mg. to 5 mg. b.i.d. (Small or emaciated patients should always be started on the lower dosage.)

The majority of patients will show optimum response on 15 mg. or 20 mg. daily, although a few may require 40 mg. a day or more. It is important to give doses that are high enough for long enough periods of time – especially in chronic patients.

Optimum therapeutic dosage levels should be reached within two or three weeks after the start of therapy. When maximum therapeutic response is achieved, dosage may be reduced gradually to a satisfactory maintenance level.

*intramuscular (for prompt control of severe symptoms):* The usual dosage is 1 mg. to 2 mg. (½-1 cc.) by deep intramuscular injection q4-6h, p.r.n. More than 6 mg. within 24 hours is rarely necessary. As soon as a satisfactory response is observed, oral medication should be substituted at the same dosage level or slightly higher.

Only in very exceptional cases should intramuscular dosage exceed 10 mg. within 24 hours. Since 'Stelazine' has a relatively long duration of action, injections should not be given at intervals of less than 4 hours because of the possibility of an excessive cumulative effect.

'Stelazine' Injection has been exceptionally well tolerated; there is little, if any, pain and irritation at the site of injection.

3. Dosage for Psychotic and Mentally Defective Children
The dosages given below apply to children, ages 6 to 12, who are either hospitalized or under adequate supervision.

*oral:* The starting dosage is 1 mg. administered once a day or b.i.d., depending on the size of the child. Dosage may be increased gradually until symptoms are controlled or until side effects become troublesome. Both the rate and the amount of dosage increases should be carefully adjusted to the size of the child and the severity of the symptoms, and the lowest effective dosage should always be used. Once control is achieved, it is usually possible to reduce dosage to a satisfactory maintenance level.

In most cases, it is not necessary to exceed 15 mg. of 'Stelazine' daily. However, some older children with severe symptoms may require, and be able to tolerate, higher dosages.

*intramuscular:* There has been little experience with the use of 'Stelazine' Injection in children. However, if it is necessary to achieve rapid control of severe symptoms, 1 mg. (½ cc.) of 'Stelazine' may be administered intramuscularly once or twice a day, depending on the size of the child. Once control is achieved, usually after the first day, the oral dosage forms of 'Stelazine' should be substituted for the Injection.

## SIDE EFFECTS

*In the dosage range of 2-4 mg. daily,* side effects from 'Stelazine' are infrequent. When they do occur, they are usually slight and transitory. Mild drowsiness occurs in a small percentage of patients; this usually disappears after a day or two of 'Stelazine' therapy. There are occasional cases of dizziness, mild skin reaction, dry mouth, insomnia and fatigue; rarely, neuromuscular reactions (extrapyramidal symptoms).

*In hospitalized psychiatric patients* receiving daily 'Stelazine' dosages of 10 mg. or more, clinical experience has shown that, when side effects occur, their appearance is usually restricted to the first two or three weeks of therapy. After this initial period, they appear infrequently, even in the course of prolonged therapy. Termination of 'Stelazine' therapy because of side effects is rarely necessary.

Side effects observed include dizziness, muscular weakness, extrapyramidal symptoms, anorexia, rash, lactation and blurred vision. Drowsiness has occurred, but has been transient, usually disappearing in a day or two.

*Neuromuscular Reactions (extrapyramidal symptoms)*
These symptoms are seen in a significant number of hospitalized mental patients receiving 'Stelazine'. They may be characterized by motor restlessness, be of the dystonic type, or they may resemble parkinsonism.

*motor restlessness:* Some patients may experience an initial transient period of stimulation or jitteriness, chiefly characterized by motor restlessness and sometimes insomnia. These patients should be reassured that this effect is temporary and will disappear spontaneously. The dosage of 'Stelazine' should not be increased while these side effects are present.

If this turbulent phase becomes too troublesome, the symptoms can be controlled by a reduction of dosage or the concomitant administration of phenobarbital or some other barbiturate.

*dystonias:* These symptoms are rare outside of mental hospitals, but they may be observed occasionally in patients who have received 'Stelazine' as a mild tranquilizer.

Symptoms may include: spasm of the neck muscles, sometimes progressing to torticollis; extensor rigidity of back muscles, sometimes progressing to opisthotonos; carpopedal spasm, trismus, swallowing difficulty, oculogyric crisis and protrusion of the tongue.

The onset of the dystonias may be sudden. A primary characteristic of these symptoms is their intermittency. They may last several minutes, disappear and then recur. There is typically no loss of consciousness and definite prodromata are usually present. Initially, these intermittent symptoms occur in a crescendo of intensity. Then as the effect of the drug wears off, the intervals between the occurrence of symptoms become longer, and the intensity of the symptoms subsides.

Despite their similarity to symptoms of serious neurological disorders, these dystonias are usually promptly reversible and need not cause undue alarm. They usually subside gradually within a few hours, and almost always within 24 to 48 hours, after the drug has been temporarily discontinued.

Treatment is symptomatic and conservative. *In mild cases,* reassurance of the patient is often sufficient therapy. Barbiturates are also useful. *In moderate cases,* barbiturates will usually bring rapid relief. The dosage and route of administration of the barbiturate used should be determined by the intensity of the symptoms and the response of the patient. *In more severe adult cases,* the administration of an anti-parkinsonism agent produces rapid, often dramatic, reversal of symptoms. Also, intravenous caffeine and sodium benzoate seems to be an effective and rapid antagonist to the dystonias. Depending on the severity of the dystonia, suitable supportive measures, such as maintaining a clear airway and adequate hydration, should be employed. *In children,* reassurance and barbiturates will usually control symptoms. Dosage and route of administration should be determined according to the intensity of symptoms and response of patient.

Note: It has been reported that injectable administration of 'Benadryl' may also be helpful in controlling dystonias.

*pseudo-parkinsonism:* These symptoms are extremely rare outside of mental hospitals.

Symptoms include: mask-like facies; drooling; tremors; pill-rolling motion; and shuffling gait.

Reassurance and sedation are important components of effective therapy. In the majority of cases these symptoms are readily reversible when an anti-parkinsonism agent is administered concomitantly with 'Stelazine'. Occasionally it is necessary to lower the dosage or to temporarily discontinue the drug.

## CAUTIONS

Clinical experience has demonstrated that 'Stelazine', a phenothiazine derivative, has a wide range of safety and that there is little likelihood of either blood or liver toxicity. The physician should be aware, however, of their possible occurrence.

One of the results of 'Stelazine' therapy may be an increase in mental and physical activity. In some patients, this effect may not be desired. For example, although 'Stelazine' has relieved anxiety and, at the same time, anginal pain in patients with angina pectoris, a few such patients have complained of increased pain while taking 'Stelazine'. Therefore, if 'Stelazine' is used in angina patients, they should be observed carefully and, if an unfavorable response is noted, the drug should be withdrawn.

Hypotension has not been a problem, but nevertheless adequate precautions should be taken when the drug is used in patients with impaired cardiovascular systems.

The antiemetic action of 'Stelazine' may mask signs of overdosage of toxic drugs or may obscure the diagnosis of conditions such as intestinal obstruction and brain tumor.

Although 'Stelazine' has shown very little potentiating activity, caution should be observed when it is used in large doses in conjunction with sedatives or depressants.

## CONTRAINDICATIONS

'Stelazine' is contraindicated in comatose or greatly depressed states due to central nervous system depressants.

## AVAILABLE

**Tablets,** 1 mg. and 2 mg., in bottles of 50, 500 and 5000. (Each tablet contains 1 mg. or 2 mg. of trifluoperazine as the dihydrochloride.)

For psychiatric patients who are hospitalized or under close supervision:

**Tablets,** 5 mg. and 10 mg., in bottles of 50, 1500 and 5000. (Each tablet contains 5 mg. or 10 mg. of trifluoperazine as the dihydrochloride.)

**Multiple-dose Vials,** 10 cc. (2 mg./cc.), in boxes of 1 and 20. (Each cc. contains, in aqueous solution, 2 mg. of trifluoperazine as the dihydrochloride, 4.75 mg. of sodium tartrate, 11.6 mg. of sodium biphosphate, 0.3 mg. of sodium saccharin, and 0.75% of benzyl alcohol as preservative.)

**Concentrate** (for hospital use), 10 mg./cc., in 2 fl. oz. bottles, in cartons of 4 and 12. (Each cc. contains 10 mg. of trifluoperazine as the dihydrochloride.)

Prescribing information adopted Jan. 1961

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# PARNATE®

brand of tranylcypromine

# PRESCRIBING INFORMATION

The physician should be familiar with the material on dosage, side effects and cautions given below before prescribing 'Parnate', and with the principles of monoamine oxidase inhibitor therapy and the side effects of this class of drugs as reported in the literature. Also, the physician should be familiar with the symptomatology of mental depressions and alternative methods of treatment to aid in the careful selection of patients for 'Parnate' therapy.

## INDICATIONS AND LIMITATIONS OF USE

'Parnate' is indicated for the relief of symptoms of mental depression which may include dejected mood, self-depreciation, lowered activity levels, difficulty in making decisions, disturbed eating and sleeping patterns, and variations of these basic symptoms as described in the literature. The therapeutic utility of monoamine oxidase inhibitors is limited specifically to depressive symptoms; these drugs may aggravate some co-existing symptoms such as agitation or anxiety.

In psychiatry, 'Parnate' is indicated in the following diagnostic categories, subject to the limitation stated above: reactive and other psychoneurotic depressions, involutional melancholia, depressive phase of manic-depressive psychosis, psychotic depressive reactions. In the psychiatric treatment of severe endogenous depressions, it is impossible to predict, with presently known data, which patients will respond best to 'Parnate' and which to ECT. 'Parnate' may be indicated in some reactive depressions in which ECT is not indicated. 'Parnate' is not recommended to treat essentially normal responses to temporary situational difficulties.

***Note:*** In depressed patients, the possibility of suicide should always be considered and adequate precautions taken. Exclusive reliance on drug therapy to prevent suicidal attempts is unwarranted, as there may be a delay in the onset of therapeutic effect or an increase in anxiety and agitation. Also, of course, some patients fail to respond to drug therapy.

## CLINICAL EXPERIENCE

Extensive clinical trials with 'Parnate' have confirmed its effectiveness and versatility. As always in the evaluation of drugs for psychic disorders, some variation in efficacy has been reported.

These studies provide the following data on the effectiveness and fundamental properties of 'Parnate':

1. In 500 patients on whom complete data are available for statistical analysis, marked or moderate improvement was reported in 77% of the nonpsychotic patients. Marked improvement was reported in 40% and moderate improvement in 27% of the psychotic patients. Some investigators have pointed out that improvement in certain instances, particularly in milder cases, may have been due to spontaneous remission of symptoms.
2. Improvement is seen within 48 hours to three weeks after starting 'Parnate'; the response can be accelerated by using higher than standard initial dosages.
3. 'Parnate' acts primarily as an antidepressant rather than as a euphoriant. Patients feel essentially normal on 'Parnate' therapy.
4. 'Parnate' can facilitate psychotherapy by increasing the patient's willingness to exert mental effort and reducing symptom-centered preoccupations.
5. 'Parnate' appears to prevent relapses in some patients who have been treated initially with ECT.

## DOSAGE

Dosage should be adjusted to the requirements of the individual patient. Dosage increases should be made only in increments of 10 mg. per day and ordinarily at intervals of one to three weeks. Side effects occur more often as dosage is increased.

Reduction from peak to maintenance dosage may be desirable before withdrawal. If withdrawn prematurely, original symptoms will recur. No tendency to produce rebound depressions of greater intensity has been seen with 'Parnate', although this is a theoretical possibility in patients treated at high dosages. Experimental work indicates that inhibition of monoamine oxidase persists for only a few days after withdrawal. Thus, any side effects due to this inhibition will probably recede rapidly upon withdrawal, which should be a distinct advantage of 'Parnate' therapy when the patient exhibits poor tolerance to antidepressant medication.

Because there is a striking relationship between dosage and speed of response, two dosage schedules are provided:

**A. Standard dosage.** (This schedule will not always produce prompt results, but it will hold the incidence of side effects to a minimum.)

1. Recommended starting dosage is 20 mg. per day — administered 10 mg. b.i.d. (morning and afternoon).
2. Continue this dosage for two to three weeks.
3. If no signs of a response appear, increase dosage to 30 mg. daily—20 mg. upon arising and 10 mg. in the afternoon.
4. Continue this dosage for at least a week.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced to a maintenance level.
6. Some patients will be maintained on 20 mg. per day; many will need only 10 mg. daily.
7. If dosages above 30 mg. daily are desired for use in exceptionally resistant cases, refer to the schedule of intensive dosage.

**B. Intensive dosage (for accelerated response).** (This schedule is for use in hospitalized patients or those under comparable supervision whenever a prompt effect is more desirable than a relative absence of side effects.)

1. Recommended starting dosage is 30 mg. per day. Administer 20 mg. in the morning and 10 mg. in the afternoon.
2. Continue this dosage for one week.
3. If no signs of a response appear, increase dosage gradually at intervals of several days to one week.
4. Dosages above 60 mg. per day are not advisable.
5. As soon as a satisfactory response is obtained, dosage may usually be reduced gradually to a maintenance level.
6. Some patients may be maintained on 20 mg. per day; many will need only 10 mg. daily.

*Note:* When ECT is being administered concurrently, 10 mg. b.i.d. can usually be given during the series, then reduced to 10 mg. daily for maintenance therapy.

## SIDE EFFECTS

**A. At standard dosages.** Side effects in patients treated with standard doses of 'Parnate' are qualitatively the same as seen at higher dosages but are generally less frequent and less severe.

The patient may experience restlessness, overstimulation, or insomnia; may notice some weakness, drowsiness, episodes of dizziness, or dry mouth; or may report nausea, diarrhea, abdominal pain, or constipation. Occasionally, headaches have occurred. Symptoms of postural hypotension have been seen most commonly, but not exclusively, in patients with pre-existent hypertension; blood pressure returns to pretreatment levels rapidly upon discontinuation of the drug. Other side effects which might occur in rare instances are tachycardia, urinary retention, significant anorexia, skin rashes, edema, palpitations, blurred vision, tinnitus, chills, paresthesia, muscle spasm and tremors, impotence, sweating and possibly paradoxical hypertension.

Most of these side effects can usually be relieved by lowering the dosage or by giving suitable concomitant medication.

**B. At intensive treatment dosages.** When 'Parnate' is used for intensive treatment to control symptoms more rapidly, an increase in the incidence and severity of side effects must be anticipated.

At doses above 30 mg. daily, postural hypotension is a major side effect of 'Parnate' therapy. It affects largely the systolic readings and occurs mainly, but not exclusively, in patients with a history of hypertension. Rare instances of syncope have been seen. Dosage increases should be made more gradually in patients showing a tendency toward hypotension at the starting dose. Postural hypotension can be relieved by having the patient lie down until blood pressure returns to normal.

Other side effects which may occur are listed above under *standard dosages*. Headaches have occasionally been severe and incapacitating. Overstimulated behavior, which may include increased anxiety, agitation and manic symptoms, can be evidence of either a side effect or an excessive therapeutic action; if this occurs, reduce dosage or administer a phenothiazine tranquilizer.

## CAUTIONS

Extensive clinical and laboratory work has shown that there is little likelihood of blood or liver toxicity. Since 'Parnate' is a non-hydrazine compound, it should prove to be exempt from the toxic effects on the liver thought to be due to the hydrazine moiety of some other drugs. However, severe toxic reactions have occurred with some mônoamine oxidase inhibitors. Pending further clinical experience, 'Parnate' should probably not be used in patients with a history of liver disease or in those with abnormal liver function tests. Drug-induced jaundice is often difficult to differentiate from other jaundice. However, there has been sufficient clinical experience with 'Parnate' to demonstrate that, if it has any potentiality for producing jaundice, the reaction must be rare. Also, the usual precautions should be observed in patients with impaired renal function since there is a possibility of accumulative effects in such patients.

Although 'Parnate' has been used in combination with various drugs (particularly Stelazine®, brand of trifluoperazine), some monoamine oxidase inhibitors have been reported to have marked potentiating effects on certain drugs, e.g., sympathomimetics, central nervous system depressants, hypotensive agents and alcohol. Therefore, the physician should bear in mind the possibility of a lowered margin of safety when 'Parnate' is combined with potent drugs and should adjust dosage carefully. 'Parnate' should not be used in combination with imipramine. (The reaction of a patient who attempted suicide with a deliberate overdosage of 'Parnate' and imipramine was more severe than would have been predicted from the properties of either drug.)

## CASES REQUIRING SPECIAL CONSIDERATION

Administer with caution to patients with recent myocardial infarction or coronary artery disease with angina of effort. Increased physical activity and, more rarely, hypotension have been reported. The pharmacologic properties of 'Parnate' suggest that it may have a capacity to suppress anginal pain that would otherwise serve as a warning sign of myocardial ischemia. When 'Parnate', like any agent which lowers blood pressure, is withdrawn from patients who tend to be hypertensive, blood pressure may again rise to undesirable levels.

When 'Parnate' is combined with a phenothiazine derivative or other compound known to affect blood pressure, elderly patients and those with cardiovascular inadequacies should be observed more closely because of the possibility of additive hypotensive effects.

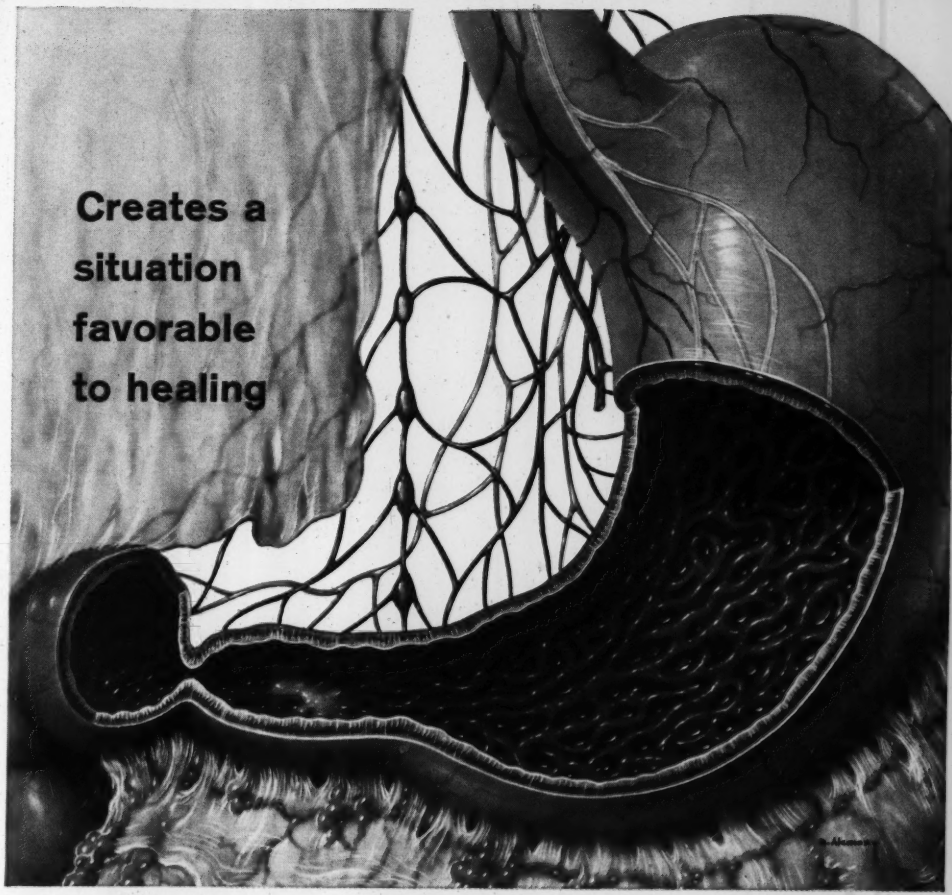
In patients being transferred to 'Parnate' from another monoamine oxidase inhibitor or from imipramine, allow a medication-free interval of one week, then initiate 'Parnate' using half the normal dosage for at least the first week of therapy. Similarly, a few days should elapse between the discontinuance of 'Parnate' and the administration of another monoamine oxidase inhibitor or of imipramine.

Because the influence of 'Parnate' on the convulsive threshold is variable in animal experiments, suitable precautions should be taken if epileptic patients are treated.

## AVAILABLE

**Tablets,** 10 mg., in bottles of 50 and 1500. (Each tablet contains 10 mg. of tranylcypromine, as the sulfate.)

Prescribing information adopted Feb. 1961




**In Pylorospasm:** 'Combid' *Spansule* capsules provide relief of psychic as well as physical factors. The anxiety, tension and apprehension that cause or complicate pyloroduodenal irritability are controlled. At the same time, the spasm itself is reduced.

'Combid' relieves irritability and hypermotility for 10 to 12 hours (all day or all night) after one dose.

SK&F

# Combid® Spansule®

brand of sustained release capsules

'Combid' *Spansule* capsules are a logical combination of 5 mg. of Darbid® (brand of isopropamide) as the iodide, a unique, inherently long-acting anticholinergic; and 10 mg. of Compazine® (brand of prochlorperazine) as the dimaleate, the outstanding tranquilizer/antiemetic in sustained release form.

Among the many conditions in which 'Combid' *Spansule* capsules are indicated are: peptic ulcer, hyperchlorhydria, pyloroduodenal irritability, irritable or spastic colon, gastric neurosis, gastritis, aerophagia, pyrosis, "nervous stomach," functional diarrhea, drug-induced diarrhea, mucous colitis, ulcerative colitis, genitourinary spasm, and nausea and vomiting of pregnancy.

DOSAGE: One 'Combid' *Spansule* capsule b.i.d. (every 12 hours). Some patients may require only one capsule every 24 hours, on arising. Only in the exceptional patient will it be necessary to increase the dosage to two capsules b.i.d. (morning and evening).

CAUTIONS AND CONTRAINDICATIONS: As is true with any preparation containing an anticholinergic, 'Combid' *Spansule* capsules should not be prescribed for patients with glaucoma, pyloric obstruction, or prostatic hypertrophy. Also, because of the antiemetic action of the 'Compazine' component (a phenothiazine derivative), 'Combid' *Spansule* capsules should not be used where nausea and vomiting are believed to be a manifestation of intestinal obstruction or brain tumor.

Clinical experience has demonstrated that 'Combid' has a wide margin of safety and that there is little likelihood of blood or liver toxicity or neuromuscular reactions (extrapyramidal symptoms). The physician should be aware, however, of their possible occurrence. When 'Combid' is used with depressant drugs, the possibility of an additive effect should be borne in mind. An occasional patient may experience mild drowsiness when first taking 'Combid'.

Prescribing information adopted January, 1961.